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FINGERNAIL GROWTH IN PREGNANCY RELATIONS TO SOME COMMON PARAMETERS OF THE REPRODUCTIVE PROCESS

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GESTATION is the epitomy of purposeful growth. The prodigious, yet orderly proliferation of fetal and maternal tissues that characterizes normal pregnancy appears to be in response to some common stimulus, shared by, if not originating in the parent organism. Whether these effects are mediated through mechanisms peculiar to pregnancy or comprise a unique and exaggerated response to factors also operative in the non-gravid state, they evidently implicate organ systems not involved primarily in the reproductive process—including the skin and its appendages. Hair growth commonly increases during pregnancy and reportedly decreases—frequently with considerable loss—following delivery. Nail growth should also be affected.

The rate of growth of fingernails has been fairly well documented in the normal, non-pregnant state (Clark and Buxton, 1938; Gilchrist and Buxton, 1939; Hamilton *et al.*, 1955; Hillman, 1955), and to a lesser extent in certain pathological conditions (Sunderland and Ray, 1952; Sharpey-Shafer, 1930; Edwards, 1938; White and Laipply, 1958; Bearn and McKusick, 1958; Luria and Asper, 1958). Differences have been noted in respect to factors of age and sex, but, thus far, not of race. Various systemic disorders as well as climatic conditions have been shown to affect not only the rate of growth, but also the quality of nail tissue elaborated (Argy, 1935; Sapin-Jaloustre and Goddard, 1959; Geoghegan *et al.*, 1958).

Review of the literature reveals only one study of fingernail growth during pregnancy. Halban and Spitzer (1929) showed the mean rate for 93 prenatal patients to be significantly greater than for non-pregnant controls. A preliminary study of 100 pregnant women also having indicated generally increased growth rates, as well as pronounced variations in individual growth patterns, the present study was designed to measure fingernail growth rates and variations during gestation, and to elucidate possible relationships to more usually recorded parameters of the reproductive process.

MATERIALS AND METHODS

The subjects were 618 patients from the maternity service of a voluntary hospital with a well supervised antepartum program. Of these, 241 women were White (78 primipara, 163 multipara); 167 were Negro (49 primipara, 112 multipara); and 210 were Puerto Rican (105 primipara, 105 multipara). Fingernail growth was measured over total periods of 14 to 252 (mean 99.7) days, at average intervals of four (minimum of two) weeks, principally during the third trimester. Additionally, growth rates were determined for 40 of these patients over periods from 38 to 181 (mean 59) days postpartum.

Linear nail growth was measured on the thumbs only by a modification of a technic previously described (Hillman, 1955). The distance between the free margin of the lunula and a distally growing mark initially inscribed on the nail over that point was determined by means of a 10X magnification microscope, with an ocular incorporated scale. Individual growth rates represented averages of all readings for both hands (rarely, data could be obtained from only one thumb). Individual variations represented mean deviations of all single period readings from the subject's overall average growth rate.

RESULTS

Results are summarized in the accompanying tables and figures. The overall nail growth during pregnancy was 120.0 ± 18.3 microns per day for White patients; 120.7 ± 17.9 microns for Negro patients; and 116.7 ± 18.5 microns for Puerto Rican patients (table 1, Fig. 1). In general, rates seemed slower after age 30, but there was no consistent relationship to parity within age and race groups.

TABLE 1

Nail growth rates of pregnant women, by ethnic group, parity and age

ETHNIC GROUP	PARITY	NO.	MEAN	S.D.	RANGE	AGE GROUP MEAN <20	20-29	30+
White	Prim.	79	124.8	19.0	82-172	123.4	125.4	120.0
	Mult.	162	117.7	17.5	74-186	111.4	123.5	114.6
Negro	Prim.	49	121.0	21.0	91-205	120.7	122.4	119.4
	Mult.	118	120.4	16.5	84-165	*	123.7	115.0
Puerto Rican	Prim.	105	116.4	16.7	73-186	116.4	117.2	115.0
	Mult.	105	117.0	21.9	67-199	*	118.6	113.6

* Fewer than 5 patients.

The differences between the mean growth rates of White and Puerto Rican primipara, between all White and all Puerto Rican patients, and between all Negro and all Puerto Rican patients were statistically significant[1] in the 20-29 year age group. The mean growth rate for 158 White patients less than 30 years of age (123.0 ± 15.1) was also significantly greater than for a comparable group of 77 non-pregnant White women (116.5 ± 16.7) (Hillman, 1955).

Mean nail growth rate was generally more rapid during the later stages of pregnancy (Fig. 2). Although extreme variation was observed, the rate increased in the third over the second trimester in 64.7% of 323 patients (mean difference 20.9 microns per day). The magnitude, but not the frequency of this increase was generally more marked among primipara; seemingly there was no relationship to maternal age. In 8 of 11 patients, the growth rate also increased from the first to the second trimester—an average gain of 8 microns per day.

[1] Statistical significance is at the 5% level unless otherwise indicated.

Among 40 patients followed postpartum (Fig. 2), the growth rate decreased in 25 (62.5%; mean 7 microns per day) below the overall rate during gestation. Among 30 of these it decreased in 27 (71.1%; mean 9 microns) below that for the third trimester. The trend seemed more pronounced among multipara, but there was no apparent relationship to race or maternal age.

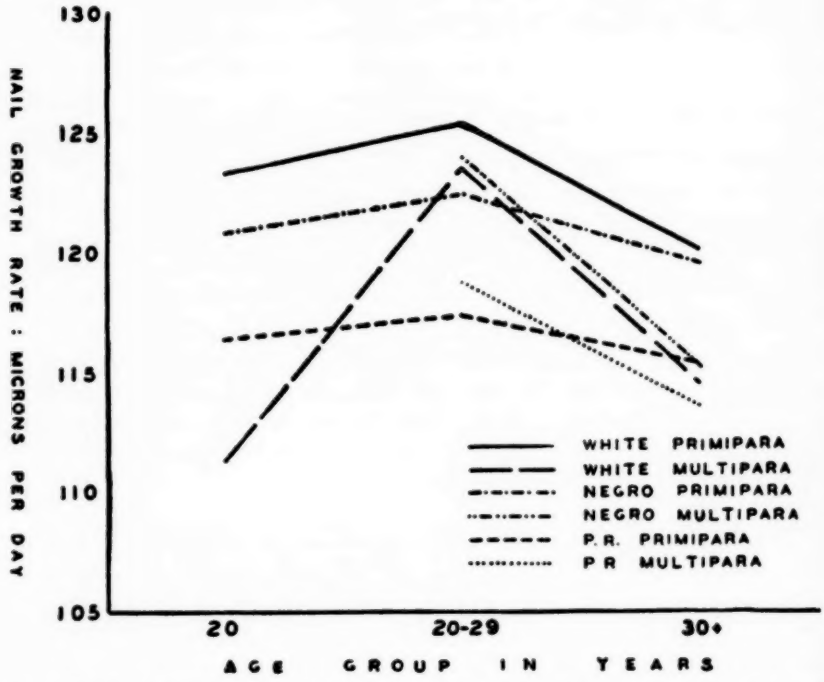

FIGURE 1. MEAN NAIL GROWTH RATES OF WHITE, NEGRO AND PUERTO RICAN GRAVIDA BY AGE GROUP AND PARITY (MINIMUM OF 5 SUBJECTS PER GROUP).

The mean individual variation in growth rate (table 2, Fig. 3) was 17.3 ± 14.5 for 122 White patients; 15.2 ± 15.2 for 126 Negro patients; and 15.1 ± 10.9 for 164 Puerto Rican patients. These averages did not differ significantly, nor was there any apparent relationship to maternal age. However, individual patient variation was significantly greater ($P < .01$) in primiparas of all racial groups, as was the ratio between variation and individual mean rate.

The difference between the mean individual variation for 182 White patients (17.3 ± 14.5) and that for a group of 89 non-pregnant White

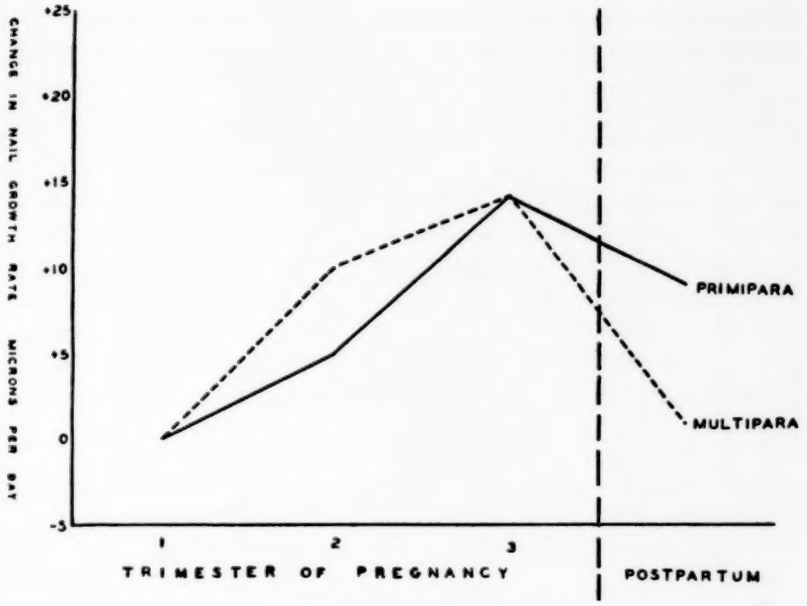

FIGURE 2. RELATIVE MEAN NAIL GROWTH RATES OF PRIMIPARA AND MULTIPARA (ALL RACES) DURING PREGNANCY AND POSTPARTUM PERIOD.

TABLE 2

Individual variation in nail growth rates of pregnant women, by ethnic group, parity and age

ETHNIC GROUP	PARITY	NO.	MEAN	S.D.	RANGE	AGE GROUP MEAN <20	20-29	30+
White	Prim.	63	18.5	14.1	2-70	18.1	16.5	23.1
	Mult.	119	15.1	14.4	2-90	*	15.1	16.0
Negro	Prim.	42	19.9	20.1	2-121	20.0	20.2	22.5
	Mult.	84	12.9	11.0	0-61	*	12.7	12.0
Puerto Rican	Prim.	90	16.2	11.1	3-68	15.0	16.5	10.5
	Mult.	74	14.7	9.6	1-49	*	14.4	11.1

* Fewer than 5 patients.

women of all ages (6.5 ± 6.1) was highly significant ($P < .001$), as was the difference between the mean variations for 118 pregnant (15.0 ± 9.7) and 63 non-pregnant (5.9 ± 5.4) White women below 30 years of age.

There was no apparent correlation between mean nail growth rate, individual variation in rate, or the ratio between these measurements

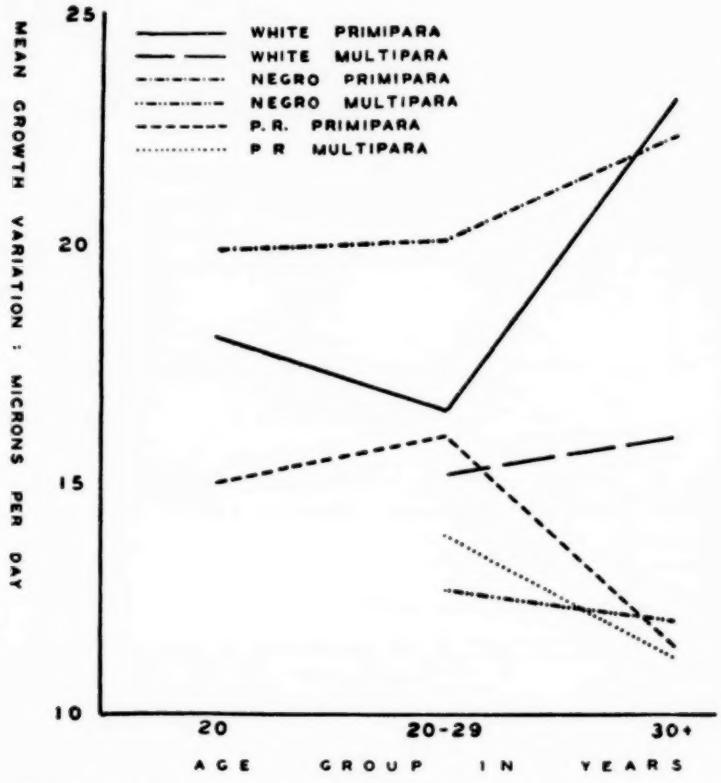

FIGURE 3. MEAN INDIVIDUAL VARIATION IN NAIL GROWTH RATES OF WHITE, NEGRO AND PUERTO RICAN GRAVIDA, BY AGE GROUP AND PARITY (MINIMUM OF 5 SUBJECTS PER GROUP).

and any of the following parameters: maternal weight at conception; maternal weight gain during pregnancy; duration of gestation; length of labor. Although variations in rate seemed strikingly increased in occasional complicated pregnancies, there was also no consistent relationship between individual nail growth pattern and the occurrence of multiple pregnancy, toxemia, difficult labor, or prematurity. However,

apparent relationships were noted to three principal indices of the reproductive process.

1) *Birth Weight.*

Birth weight, not birth length, seemed related to both mean growth rate and to mean individual variation, and these associations appeared influenced by the factor of race (tables 3, 4, Figs. 4, 5). Among White multipara 20 to 29 years, the average birth weight of all children—of previous and present pregnancies—of mothers with rates above the group average was significantly higher ($P < .01$) than for those with lower than average rates of growth (table 3, Fig. 4). Among Negro and Puerto Rican multigravida in the same age group, the mean birth weight was significantly lower for all children of mothers with above average nail growth rates. The difference between the mean weight of children of

TABLE 3

Mean birth weights of all infants of multipara (total pregnancies) in relation to mean nail growth rate and individual variation, by race and sex

PATIENT		RATE *		VARIATION **	
		Below Average	Above Average	Below Average	Above Average
White	Male	7.46	7.50	7.71	7.44
	Female	7.90	7.65	7.38	7.33
	Total	7.16	7.58	7.54	7.38
Negro	Male	7.28	7.26	7.39	7.34
	Female	7.30	6.86	7.36	6.81
	Total	7.29	7.05	7.38	7.01
Puerto Rican	Male	7.56	7.38	7.41	7.76
	Female	7.29	6.94	6.84	7.37
	Total	7.40	7.13	7.18	7.54

* Patients 20-29 years of age. ** Patients in all age groups.

White mothers and those of Negro and Puerto Rican mothers with nail growth rates above average was highly significant ($P < .001$). This difference was referable chiefly to differences in the weights of female infants; significant variations in relation to maternal nail growth rates were not found in the weights of male newborns (table 3, Fig. 4).[2]

[2] Mean birth weights for all infants of mothers in each of the three racial groups did not differ significantly.

Although fertility and parity per se appeared not to influence this relationship, the observed associations seemed referable in part to consistent weight patterns in successive children of polygravida.[3] For current pregnancies only, the mean birth weights of infants born to both primi-

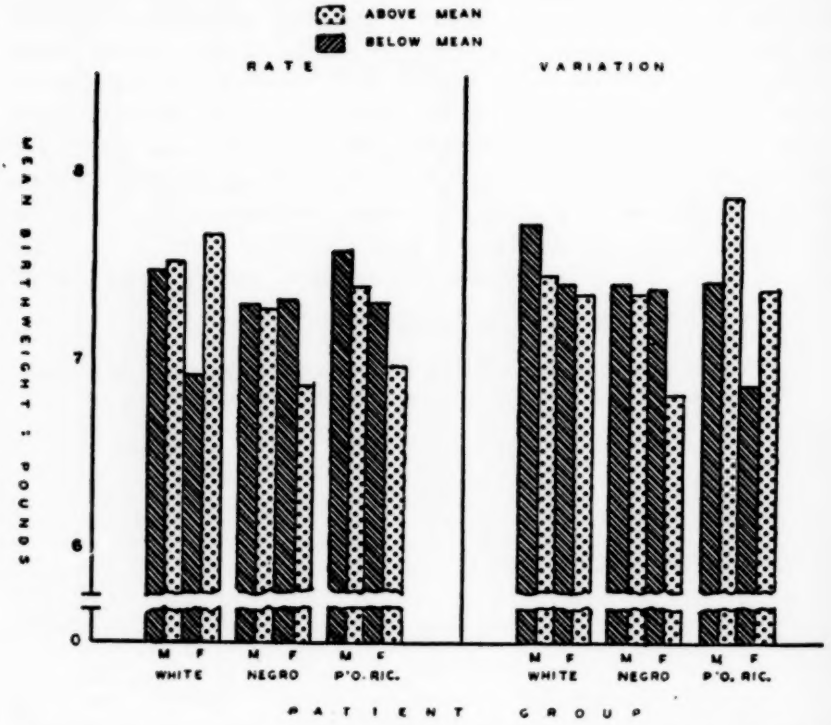

FIGURE 4. MEAN BIRTH WEIGHTS OF ALL CHILDREN OF MULTIPARA 20-29 ACCORDING TO MATERNAL NAIL GROWTH PATTERN, BY RACE AND SEX.

para and multipara seemed generally less related to nail growth rate (table 4, Fig. 5). Although the difference between the mean birth weights of infants of those women with rates respectively below and above the mean was statistically significant for the White patient group ($P < .01$), it was not significant for the Negro and Puerto Rican groups

[3] Maternal smoking habits, reportedly associated with differences in infant birth weight, showed no consistent relationship to nail growth patterns. Smokers showed a higher frequency of nail biting than non-smokers. Nail biters tended to have more rapid nail growth rates among white patients.

TABLE 4

Mean birth weights of infants of all patients (current pregnancy only) in relation to mean nail growth rate, by race and sex

PATIENT GROUP	INFANT SEX	BELOW MEAN			ABOVE MEAN		
		Primip.	Multip.	Total	Primip.	Multip.	Total
White	Male	7.03	7.18	7.14	6.75	7.62	7.25
	Female	7.05	6.68	6.80	7.47	7.87	7.75
	Total	7.04	6.96	6.98	6.92	7.75	7.48
Negro	Male	6.54	6.81	6.75	7.08	7.38	7.27
	Female	6.20	7.29	6.82	6.37	6.68	6.61
	Total	6.34	7.05	6.78	6.75	7.01	6.93
Puerto Rican	Male	7.21	7.14	7.18	7.12	7.83	7.45
	Female	6.86	7.69	7.24	6.67	7.33	7.03
	Total	7.04	7.41	7.21	6.92	7.51	7.20

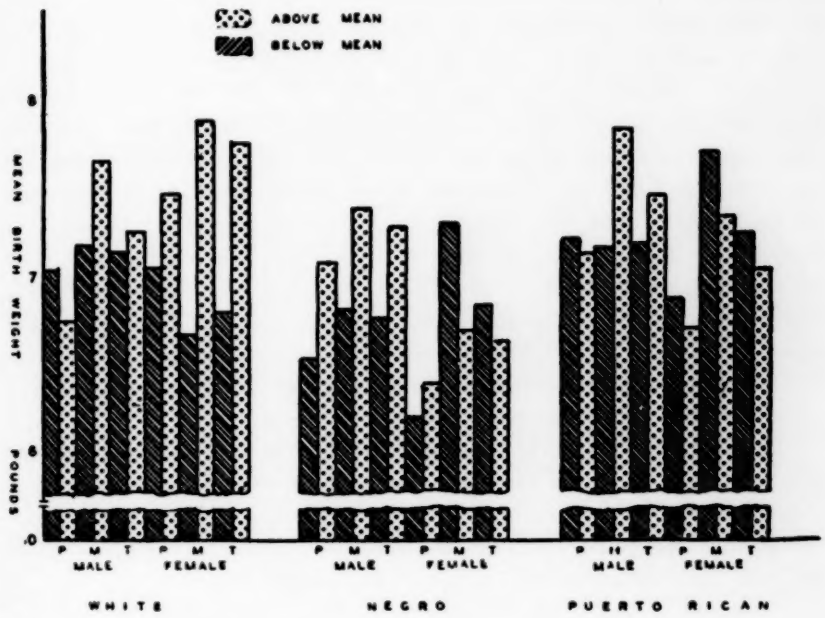

FIGURE 5. MEAN BIRTH WEIGHTS OF INFANTS OF PRIMIPARA AND MULTIPARA 20-29 ACCORDING TO MATERNAL NAIL GROWTH RATE, BY RACE AND SEX. (P: primipara M: multipara T: total).

(individually or combined). The difference between the mean weight of infants born to White patients with rates above the mean and that of infants born to Negro and Puerto Rican mothers with above average rates was just barely significant.

In respect to individual variation in nail growth rate, the mean birth weight of children of all White and Negro multiparas was significantly higher among mothers below, than those above average. An opposite tendency in children of Puerto Rican multipara was not statistically significant, but the difference between this group and the combined White and Negro groups was significant. There was no apparent relationship to the sex of the offspring. However, there was a suggestion of positive association between overall fertility and both growth rate and variation, in all three racial groups.

2) *Sex Ratio.*

The secondary sex ratio also seemed related to the overall rate of nail growth and (indirectly) to the variation/rate ratio, though not to individual variation per se (table 5, Fig. 6). Comparable to those noted for birth weight, associations between nail growth patterns and the sex ratio at birth seemed more evident in data for all progeny of multipara as well as affected by the factor of race. In both White and Negro multipara, the sex ratio for total births appeared higher among women with nail growth rates above the mean. In Puerto Rican multipara, the sex ratio was lower in patients above the mean—a difference just short of significance. For the White and Negro multipara, the sex ratio was significantly lower among patients with varation/rate ratios above their respective means. Among Puerto Rican multigravida, the sex ratio was higher (though not significantly) for patients with variation/rate ratios above the mean. The difference between the sex ratios for Puerto Rican and the combined White and Negro groups was significant among individuals with variation/growth ratios above the mean.

For White and Negro children of current pregnancies only (primipara and multipara), the sex ratio remained significantly lower among those with variation/rate ratios above average. However, the difference between this ratio and that for all current offspring of Puerto Rican patients with variation/rate ratios above average was not significant.

3) *Abortion.*

In almost reciprocal fashion, and with racial factors again seemingly operative, the nail growth pattern seemed related to the occurrence of

TABLE 5

Sex ratio and frequency of abortion in relation to mean nail growth rate, variation and variation/rate ratio, by race

PATIENT GROUP	SEX RATIO *					
	RATE **		VARIATION **		V/R RATIO **	
	Below	Above	Below	Above	Below	Above
White	0.980	1.221	1.098	1.030	1.144	0.949
Negro	0.852	1.081	0.924	0.674	1.011	0.614
Puerto Rican	1.231	0.849	1.096	0.957	1.000	1.182

PATIENT GROUP	ABORTION †					
	RATE		VARIATION		V/R RATIO	
	Below	Above	Below	Above	Below	Above
White	25.4 (11.7)	16.0 (7.4)	19.2 (10.1)	18.4 (6.2)	19.5 (10.1)	17.2 (8.0)
Negro	27.1 (13.2)	20.0 (11.8)	22.0 (14.3)	24.3 (15.4)	23.7 (14.0)	26.2 (10.3)
Puerto Rican	14.3 (7.7)	14.1 (8.5)	13.6 (7.9)	9.8 (7.2)	16.0 (9.5)	7.9 (5.9)

* Ratio of all infants born to all patients

** Relation to mean for respective racial group.

† Percent of all patients with history of previous abortion; and (in parenthesis) relative frequency of abortions to total pregnancies.

abortion (table 5, Fig. 6). Associations were noted between the total frequency of abortion (ratio of total abortion to total pregnancies) and both nail growth ratio and the variation/rate ratio, but not to variation per se. Seemingly stronger relationships were also observed between these parameters and the proportion of patients with a previous history of miscarriage, suggesting a repetitive phenomenon in susceptible individuals.[4]

In both White and Negro groups, a history of abortion was more common among patients with growth rates below than above the mean (those with a lower sex ratio), a difference just short of statistical significance. In Puerto Rican patients the proportion of mothers with a history of previous miscarriage was approximately the same in both groups. However, the frequency of abortion history among patients

[4] Among all patients, the sex ratio for those with a history of miscarriage (0.903) was lower than for those with no history of miscarriage (1.047). The difference was not statistically significant ($P > .05$).

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with nail growth rates below the mean was significantly higher in Whites and Negroes than in Puerto Ricans.[5]

Associations between a history of abortion and the variation/rate ratio were generally of a higher order of probability. The White patient group

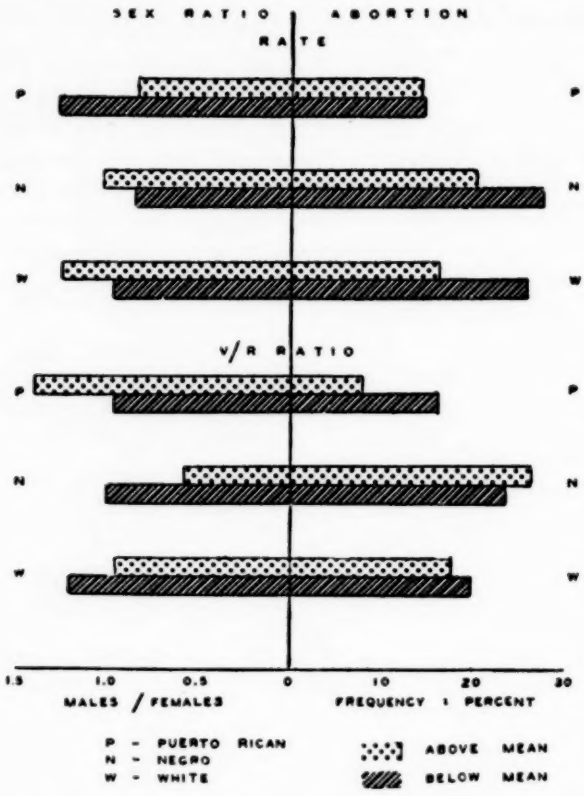

FIGURE 6. RELATION OF SEX RATIO AND FREQUENCY OF ABORTION HISTORY TO NAIL GROWTH PATTERN IN MULTIPARA, BY RACE.

showed a slightly lower, and the Negro group a slightly higher history of miscarriage in patients above the mean. The Puerto Rican group had a substantially, though not significantly, lower frequency of histories "positive" for miscarriage in patients above the mean. However, the

[5] The overall abortion rate for Negro patients was significantly greater ($P < .05$) than that for Puerto Rican gravida, but differences between these frequencies and the rate for White mothers was not significant.

difference between this group and the combined White and Negro groups was statistically significant. Variation per se seemed unrelated to the abortion rate.

The frequency of estimated total complications (maternal and fetal, of pregnancy and labor, during previous and present pregnancies) was significantly higher among White and Negro multipara (combined group) with growth rates above the mean. No appreciable difference was noted among Puerto Rican patients in respect to mean growth rate, nor did the frequency of total complications for patients in this group differ significantly from that for the combined White and Negro groups. Total complications also tended to be more common among White and Puerto Rican, but not Negro, patients with growth variation above the mean.

In general, nail growth rates among patients with blood group A were faster than among patients with group O blood—notably among Puerto Rican gravida—but the difference was not statistically significant. Growth variation showed no consistent relationship to patient blood group. Racial differences in growth rates were not attributable to racial differences in the frequencies of ABO blood groups. Nail growth patterns appeared unrelated to the occurrence of the Rh blood factor.

DISCUSSION

The present findings are in accord with those of Halban and Spitzer (1929) in demonstrating an increased rate of fingernail growth during pregnancy. Conceivably, the differences between growth rates in pregnant and non-pregnant women might reflect basic constitutional factors governing, among other attributes, the ability to conceive. However, the observed general tendency to reduced growth rates among patients followed postpartum reinforces the impression that the increased rate is probably the result of, rather than an index of capacity for, pregnancy.

Hypothesized relationships between nail growth and total metabolism are supported by the usually more rapid rates noted in the last trimester, and the observation that overall nail growth rates during pregnancy exceed those in the normal male, which, in turn, are greater than those in the non-gravid female (Hillman, 1955). The apparent lack of correlation between nail growth and fetal length, maternal weight, or maternal weight gain during gestation, constitute possible negative evidence. However, as in the failure to demonstrate a relationship between nail growth and body size in non-pregnant subjects (Hillman, 1955; Hamilton *et al.*, 1955), absence of correlations may be referable to insuffi-

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cient observations on a highly variable characteristic (as well as failure to consider lean body mass).

The significantly lower nail growth rates of the (generally smaller) Puerto Rican patients are perhaps also consistent with the concept of a relationship to total metabolism, although impressions concerning fundamental racial differences must be validated by observations on non-pregnant individuals. Moreover, nail growth among the Japanese has been reported comparable to that in Caucasians (Hamilton *et al.*, 1955). Local environmental conditions also exert an influence, presumably through effects on digital circulation (Geoghegan *et al.*, 1958; Sapin-Jaloustre and Goddard, 1956).

The marked increase in intra-individual variation in rate seems the most distinctive aspect of the altered nail growth pattern in pregnancy. In the light of generally greater variations observed in non-gravid females compared with males (Hillman, 1955), these significantly augmented deviations from average growth rates may be related to the increased hormonal activity characteristic of gestation.

Apparent relationships between nail growth patterns and such phenomena as infant birth weight, sex ratio and the frequency of abortion are provocative though not readily explained. Moreover, their validity is suspect by reason of dependence in part on patient recall, rather than on objectively substantiated information. The relatively low figure for the overall frequency of abortion among the Puerto Rican group especially suggests serious limitations to these and other data derived chiefly from patient histories. However, since reliability of reporting would seem unrelated to nail growth—hence randomly distributed—at least some of these associations are probably real rather than spurious.

The apparent association between nail growth patterns and the secondary sex ratio may be practically meaningful, particularly in the light of seeming converse associations between these same measurements and an apparent tendency to abort. This reciprocal relationship—generally consistent even in respect to racial patterns—is in accord with evidence for a progressively declining sex ratio following conception (Lowe and McKeown, 1950). Since it is most evident in successive pregnancies of individual multipara, it may also indicate basic constitutional differences in the ability to carry a pregnancy to term, notably in the case of the less viable male fetus. A study of the sex ratio in relation to usually accepted indices of total metabolism—*e. g.* among children of women with thyroid disorders—might contribute relevant information.

SUMMARY

Fingernail growth rates and variations were measured in 618 pregnant women, including 241 White, 167 Negro and 210 Puerto Rican subjects.

The mean growth rates and mean individual variations in rate were significantly greater in the prenatal group than rates reported for nonpregnant women.

In general, the mean growth rates were most rapid in the third trimester, and declined during the postpartum period.

Nail growth rates seemed influenced by factors of race and age, but not of parity. Variations in rate appeared related to parity, but not to race or age.

Maternal nail growth rates and variation/rate ratios seemed related to infant birth weight, the secondary sex ratio, the frequency of abortion, and, possibly, to total complications. They appeared unrelated to birth length, maternal weight, or to the occurrence of toxemia and other complications.

ACKNOWLEDGMENT

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VENOMOTOR REACTIONS IN THE FOREARM VEINS OF MAN *

BY GERMAN MALARET, ANTONIO QUIROZ AND G. E. BURCH **

A simple method for measuring venomotor reactions was recently described by Burch and Murtadha (1956) using an isolated intact venous segment in the forearm of man. Other observers have employed similar techniques.[1] The method produced minimal physiologic disturbances while studying the behavior of the venous segment. Although the responses are recorded quantitatively it is not always possible to compare them satisfactorily in different subjects or in the same subject at different times because (1) the preparation varies from subject to subject, and (2) subjects react differently in degree in each experimental preparation. Nevertheless, the veins are extremely active and satisfactory quantitative measurements can be recorded. Considering that 60% to 75% of the blood is found in the venous side of the circulatory system, these venomotor reactions are important since they may shift large quantities of blood under appropriate circumstances. In an effort to understand venomotor reactions more clearly, a series of experiments were conducted on the isolated venous segment of the forearm of man. This report is concerned with the results of those experiments.

MATERIALS AND METHODS

Thirty-five subjects were studied (tables 1 and 2) which included 28 Negro males, one Negro female, and six white males, ranging in age from 15 to 64 years. Eleven of the 35 subjects had clinical evidence of chronic congestive heart failure (CHF), four of whom were fairly well compensated. Three of the subjects with chronic CHF were tested twice. Of the 24 subjects free of congestive heart failure (control subjects), one had nephrosis and one had a large aneurysm of the ascending aorta which partially obstructed the superior vena cava. All subjects rested supine in a hospital bed in a quiet room. It was necessary to elevate the heads of some of the patients with congestive failure.

* Aided by grants from the U. S. Public Health Service.

** From Tulane University School of Medicine, Department of Medicine, and Charity Hospital of Louisiana, New Orleans, Louisiana.

[1] Duggan, *et al.*, 1953; Martin, *et al.*, 1959; Page, *et al.*, 1955.

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TABLE 1

The male control subjects

SUBJ. NO.	AGE YEARS	MEAN SVP BEFORE ISOLATION (mm. H_2O)	MEAN SVP AFTER ISOLATION (mm. H_2O)	MEAN PVP (mm. H_2O)	DIAGNOSIS
1	32	110	160	—	Hemorrhoids
2	62	80	370	—	Resolving pneumonia
3	46	130	155	—	Resolved pneumonia
4	34	114	133	—	Duodenal ulcer
5	17	130	385	—	Neurofibroma
6	33	115	175	135	Diabetes Mellitus
7	27	115	200	125	Duodenal ulcer
8	55	100	330	100	Inguinal hernia
9	45	165	190	150	Nephrosis
10	42	125	240	115	Seborrheic dermatitis
11	17	140	215	115	No disease
12	36	190	225	80	Resolved pneumonia Repaired VSD
13	46	80	190	125	Diabetes Mellitus
14	36	160	235	90	Nephrocalcinosis
15	52	260	295	235	Aneurysm of Ascending aorta
16	15	160	360	80	? Glomerulonephritis
17	25	140	220	155	Pylorospasm
18	59	138	247	183	Primary amyloidosis
19	31	135	180	130	Essential hypertension
20	24	162	238	145	Diabetes Mellitus
21	48	125	200	130	Inguinal hernia
22	40	100	160	—	Arthralgia
23	27	162	260	140	Pylorospasm
24	44	130	250	100	Thalasemia Minor
	MEAN	133	230	129	

Venous pressures and clinical diagnoses in the 24 male control subjects studied. Six subjects were White and 18 Negro. The mean values exclude subject 15 who had partial obstruction of the superior vena cava causing an elevated baseline venous pressure.

The subjects were chosen because of the presence of prominent forearm veins with satisfactory segments for isolation. The segment was considered adequate if (1) after being occluded proximally and distally it failed to empty on digital pressure over the isolated venous segment, (2) after being occluded distally and emptied proximally it failed to fill, (3) after being emptied from the midpoint proximally and distally it failed to fill, and (4) the pressure within the segment remained above that in the systemic veins throughout the experiment. The segments

used were free from valves as well as tributaries and their lengths varied from 2.5 to 6.0 cm.

Care was taken to eliminate any constricting clothing which might alter the measurement of the venous pressure. The subject's arm rested comfortably on a table at the phlebostatic level and was supported by

TABLE 2

The subjects with congestive heart failure

SUBJ. NO.	AGE YEARS	MEAN SVP BEFORE ISOLATION (mm. H_2O)	MEAN SVP AFTER ISOLATION (mm. H_2O)	MEAN PVP (mm. H_2O)	DIAGNOSIS
25	58	220	350	—	ASHD
26	45	100	—	100	Luetic HD
	45	550	600	225	Luetic HD
27	63	305	500	280	ASHD
28	57	310	340	300	Luetic HD
29	51	320	370	250	HCVD, Myocarditis
30	25	250	315	250	RHD
	25	385	475	435	RHD
31	55	170	360	175	Cor Pulmonale
32	30	170	240	165	HCVD
33	36	190	370	160	Myocarditis
34	64	123	193	100	ASHD
35	32	340	410	340	RHD
	32	320	495	345	RHD
	MEAN	270	350	242	

Venous pressures and diagnoses in subjects with congestive heart failure. Note that subjects 26, 30 and 35 were studied twice each on separate days. The mean values exclude subject 26 who had a very variable venous pressure due to Cheyne-Stokes respiration. ASHD—arteriosclerotic heart disease; HCVD—hypertensive cardiovascular disease; RHD—rheumatic heart disease; HD—heart disease.

sand bags. The venous pressure was measured with a 24-gauge hypodermic needle connected via a Statham strain gauge pressure transducer to a satisfactory multichannel direct writing recorder.

In 32 subjects the venous pressure was measured concurrently in the same manner in a superficial median basilic vein open to the systemic venous system, although occasionally a smaller forearm vein was used. Care was taken not to use the same forearm vein for both the isolated segment and the open systemic vein. To prevent clotting the transducers,

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the polyethylene tubing and the needles were filled with a solution of heparin and saline (1 mg heparin in 10 cc normal saline) and the tip of the needle was immersed in undiluted heparin. Once the occluding brass wedges were applied no further adjustments were made unless absolutely necessary. In four subjects the arterial blood pressure was recorded continuously with an intraarterial needle inserted in the brachial artery in the arm opposite the segment, by means of a Statham strain gauge pressure transducer and the multichannel direct writing recorder. In the remaining subjects, arterial blood pressure and pulse and respiratory rates were recorded intermittently by one of the observers.

Two hundred and eighty studies were obtained. In a few instances, the experiments had to be discontinued because of spasm in the venous segments.

RESULTS

Isolation of the Segment. After a satisfactory record was obtained of the normal venous pressure in the segmental vein and in the open peripheral vein the proximal occlusion of the segment was made. This resulted in an increase in the segmental venous pressure of from 0 to 75 mm H_2O, the mean being 27 mm H_2O and 23 mm H_2O, respectively, for the control subjects and the patients with congestive heart failure. The distal occlusion was then made and the segmental venous pressure (SVP) allowed to stabilize. The total mean rise was 97 mm H_2O for the control subjects and 103 mm H_2O for the patients with congestive heart failure (Fig. 1).

Spontaneous variations in venous pressure due to the pulse and respiration were noted before application of the occluding wedges. These spontaneous fluctuations in venous pressure varied considerably in magnitude being greater in anxious and tense subjects. After the application of the occluding wedges, deflections in pressure due to the pulse remained essentially unchanged or diminished in size, whereas the deflections in pressure due to respiration disappeared from the isolated venous segment in practically all subjects. It appears, therefore, that the respiratory variations in venous pressure are associated primarily with the changes in intra-thoracic pressure.

It was also noted that the smaller veins had higher pressures than the larger ones. Thus, the peripheral venous pressure (PVP) was usually lower than the segmental venous pressure prior to the application of the wedges. In the few cases where the peripheral vein left open to the systemic venous circulation was smaller than the segmental vein, the

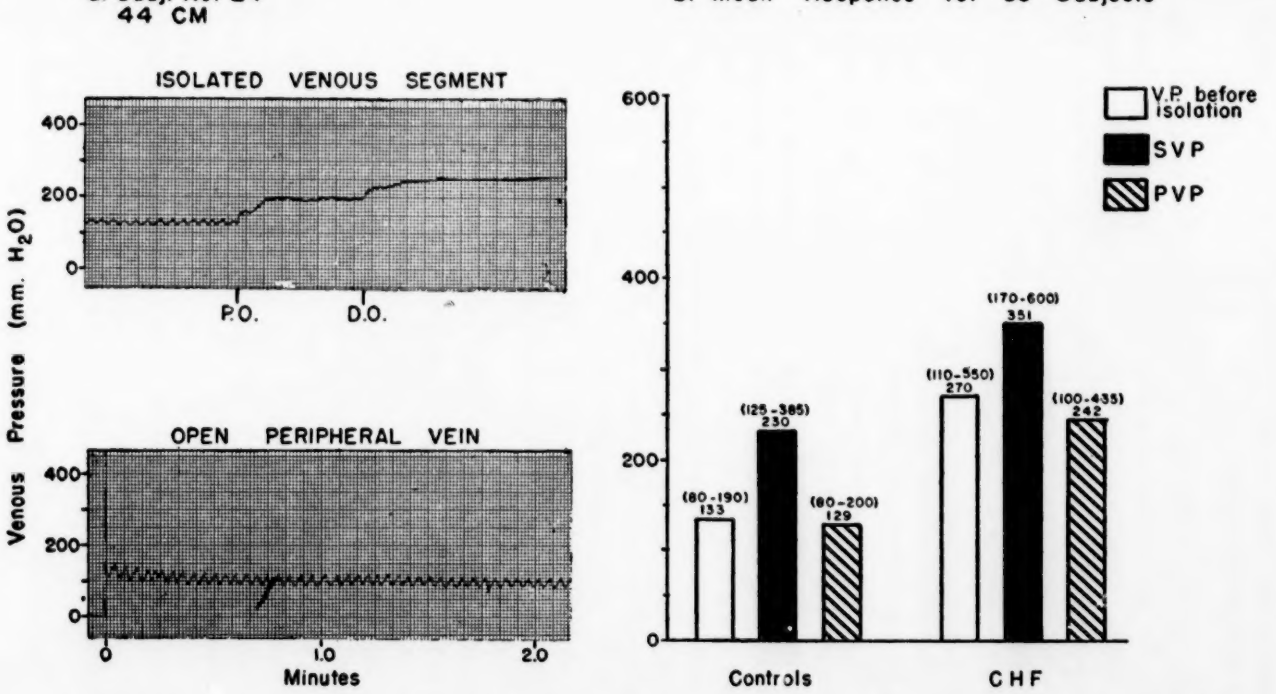

FIGURE 1(a). An original tracing showing the changes in pressure in the venous segment with application of the occluding brass wedges. (b) The mean venous pressure change produced by isolation of the venous segment. In this and all illustrations with bar graphs the mean value is shown at the top of the bar and the range in the parentheses.

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venous pressure was higher in the former than in the latter, which is in agreement with previous studies.[2]

Stroking the Skin. The skin over the isolated segment was stroked gently with the smooth end of a glass rod in five control subjects and four with CHF. Twenty-one observations were made and the means for both groups are shown in Figure 2. Of the eight observations in the control subjects, two showed no change, two showed an increase and four showed a decrease in venous tone. The increase occurred in segments where a visible ring of venous spasm developed during stroking, presumably as a result of local injury near the needle tip when the overlying glass rod pinched the wall of the vein against the needle in the lumen. In both instances, the spasm subsided after a short time. In one of the two subjects in whom no change occurred, the SVP was 600 mm H_2O initially, suggesting a marked increase in venous tone due to an unknown factor. In the other four observations, the mean decrease in SVP was 20 mm H_2O (range 5 to 75 mm H_2O). Spasms never developed when the stroking was gentle and the wall of the vein was not traumatized.

There were 13 observations in the patients with CHF. Eleven had a decrease and two an increase in the SVP. The two in whom there was an increase included a subject with a spastic segment and a subject with a steadily rising venous pressure both in the segment and in the open peripheral vein which was not stroked. In the 11 instances with a decrease in venous tone the range of decline was 25 to 270 mm H_20, the mean being 107 mm H_2O.

The mechanism of venous relaxation following stroking of the overlying skin is not known. It has been postulated that it may be due to a local reflex, to the local release of chemical agents or to strictly physical influence upon the smooth muscle of the vein. Note the difference in the degree of response in the patients with CHF and in the control subjects. It appears that the veins in the former group, being in a state of higher tone, were able to relax more on appropriate stimulation. This difference was also noted following administration of hexamethonium (*vide infra*).

Hexamethonium. Varying doses of hexamethonium (Bistrium Bromide) were injected intravenously in the opposite arm of six control subjects and five patients with CHF. In all but two control subjects

[2] Burch, 1954b; Gauer and Sieker, 1956; Oschner, *et al.*, 1951; Wallace and Stead, 1957.

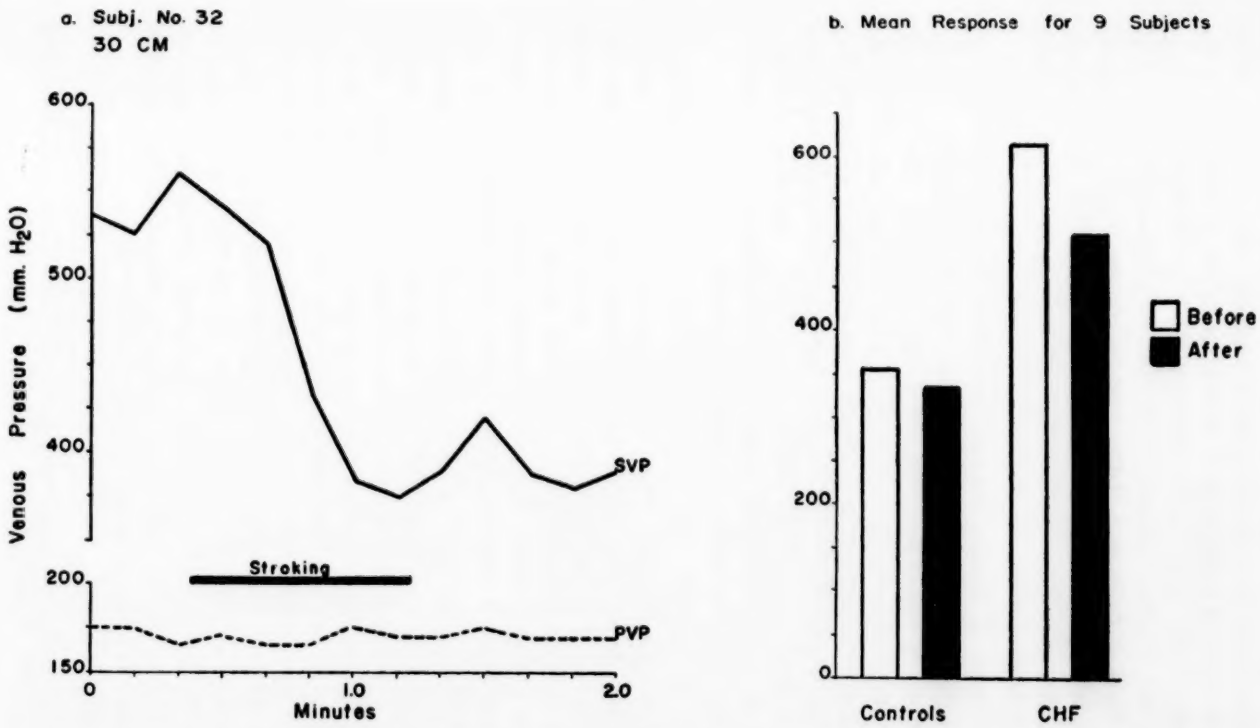

FIGURE 2(a). The effect of stroking the skin over the isolated venous segment with a smooth end glass rod on segmental venous pressure (SVP). (b) The bar graph illustrates the mean change in SVP in control subjects and the patients with congestive heart failure.

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a decrease in venomotor tone occurred. The decrease was greater in the subjects with CHF than in the control subjects (Fig. 3). The doses varied from 2.5 to 5.0 mg of hexamethonium in 12 observations on the patients with CHF. The average decline in SVP was 66 mm H_2O (range 20 to 200 mm H_2O). Concomitantly, the PVP decreased an average of 24 mm H_2O (0 to 50 mm H_2O), with no change in one instance and a rise of 5 mm H_2O in two instances. All subjects with CHF felt considerably better after the administration of the drug, and in some patients the clinical improvement was dramatic.

Larger doses of hexamethonium were used in the control subjects (5 to 25 mg). The changes in venomotor tone were variable. In one subject 20 mg of hexamethonium caused no change; in another 25 mg was associated with a steady rise in SVP with no change in PVP; and the remaining four subjects had a mean decrease in SVP of 17 mm H_2O (range 0 to 50 mm H_2O). This is in agreement with the findings of Burch and Murtadha (1956) and Burch (1955). Actually, the mean decrease in SVP in the control subjects was distorted by the inclusion of a single instance of a marked decrease in pressure.

In both groups, the arterial blood pressure was recorded sphygmomanometrically in the opposite arm at 30-second intervals. The systolic blood pressure declined by an average of 13 mm Hg (0 to 36 mm Hg) and the diastolic pressure by 3 mm Hg (0 to 10 mm Hg). Although the venous pressure returned very gradually to the pre-injection level, the arterial blood pressure returned promptly, a finding in agreement with previous studies (Burch and Murtahda, 1956; Burch, 1955.).

The mechanism of action of hexamethonium is well established. In the doses used in this study the block of the sympathetic innervation was not complete since a response could still be elicited on appropriate stimulation. Judging from the improvement in the subjects with CHF, it can be stated again that hexamethonium used judiciously is definitely beneficial in the treatment of CHF. The improvement and sensation of well-being followed the decrease in venomotor tone which in turn was associated with a decrease in venous return to the heart and lungs, thus lightening the load on the heart and decreasing pulmonary congestion. This observation has been made previously by other observers who used various ganglionic blocking agents.[3]

[3] Burch and Murtahda, 1956; Burch, 1954a, 1955, 1956; Burch and Ray, 1954; Kelley, *et al.*, 1953; Shuman, 1950.

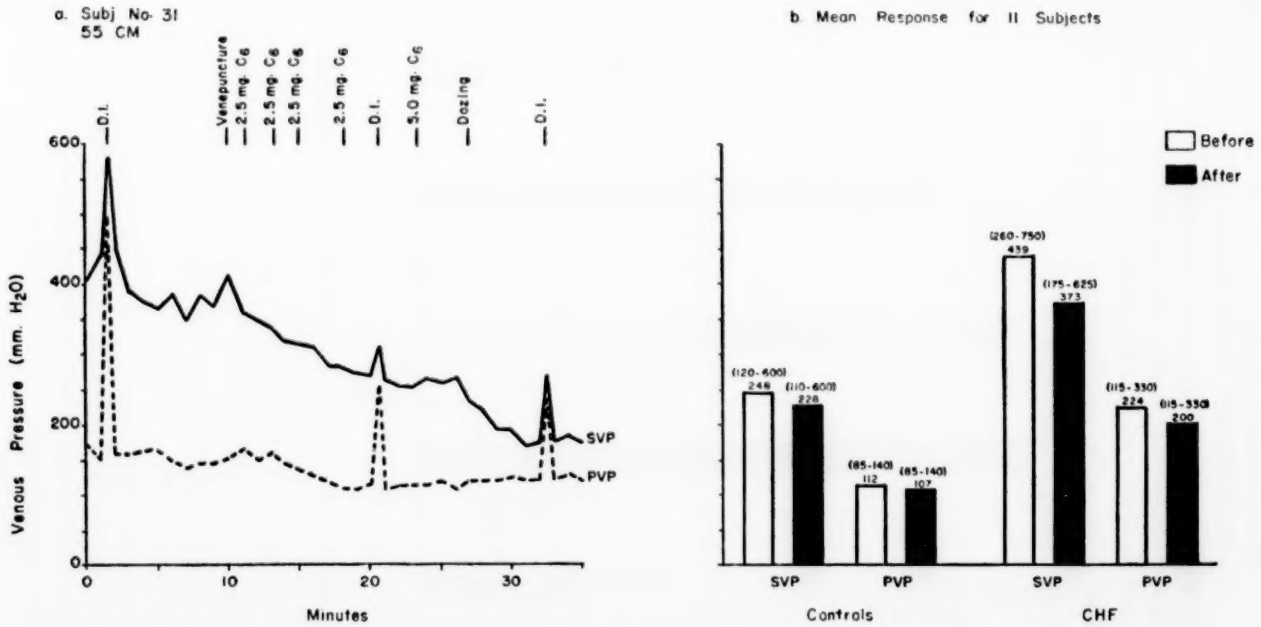

FIGURE 3. Effect of intravenous administration of hexamethonium (C_6) on venous pressure. Note that the venous pressure decreased in both the isolated venous segment and the open peripheral vein. Note, also the reduction in magnitude of the venoconstrictor response following deep inspiration (D. I.).

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Noradrenalin. Noradrenalin was injected directly into the isolated segment in five subjects, three control and two with CHF (Fig. 4). In all instances the SVP increased rapidly and markedly following a brief decrease in pressure. The amount of noradrenalin used was 0.05 cc of a solution prepared by diluting 0.2 cc of a 0.2% solution of noradrenalin in 50 cc of normal saline. The brief decrease in SVP was attributed to

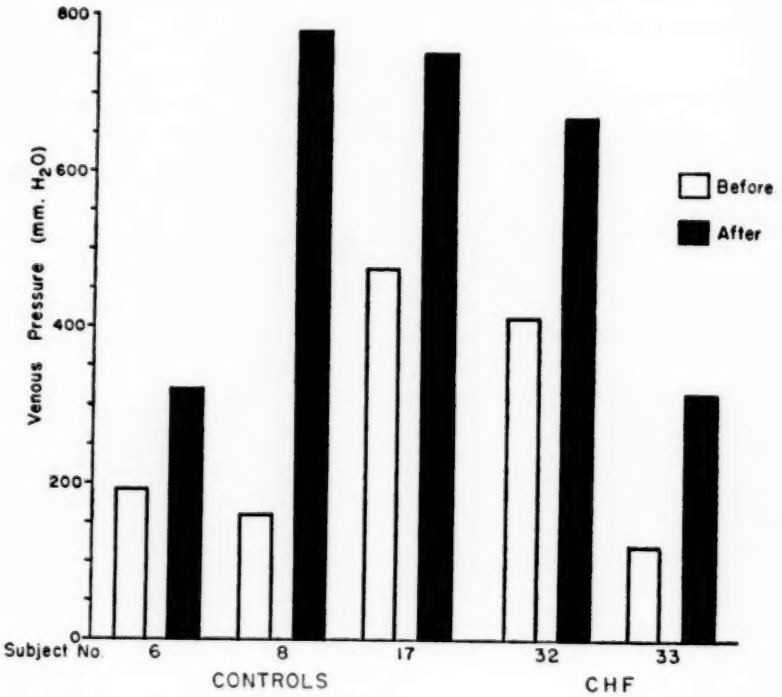

FIGURE 4. Effect of noradrenalin injected directly into the isolated venous segment.

the suction effect of the syringe while entering the vein. Once the noradrenalin was injected, the response was rapid. In order to eliminate the possibility that the pressure response was due to the volume of fluid injected into the isolated segment, the same amount of normal saline (0.05 cc) was injected into a segment which caused a small increase in SVP (50 mm H_2O or less). In other instances an equal volume of blood was removed from the segment after the noradrenalin had been injected but the response was the same.

In three additional subjects noradrenalin was injected intravenously in the opposite arm by an infusion prepared by diluting 2.0 cc of a 0.2% solution in 500 cc of normal saline. The arterial blood pressure was recorded continuously by means of Statham transducers simultaneously with the recording of venous pressure in two subjects and at 30 second

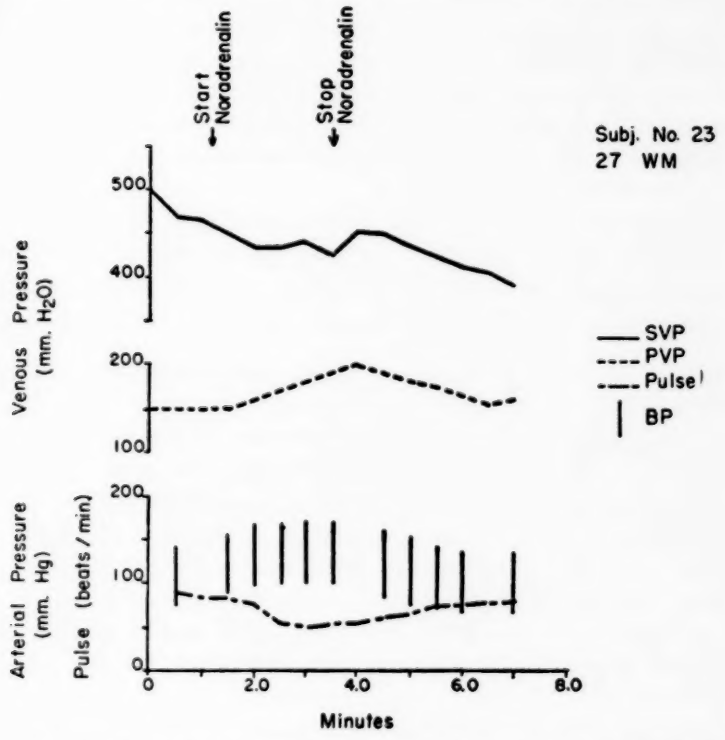

FIGURE 5. Effect of noradrenalin injected intravenously in an open systemic vein. Note the decrease in segmental venous pressure (SVP) and pulse rate and the associated increase in peripheral venous pressure (PVP) and arterial blood pressure.

intervals with a sphygmomanometer in the third subject. Figure 5 shows a representative example of the response to noradrenalin. The arterial blood pressure increased an average of 33 mm Hg, systolic, and 19 mm Hg, diastolic. In all five experiments on the three subjects, the peripheral venous pressure increased steadily and the pulse rates declined until the noradrenalin was discontinued. The response of the SVP varied, increasing in two and decreasing in three instances. The fact that the

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PVP rose in all instances is further evidence of the direct effect of noradrenalin on the smooth muscle of the veins. The same response was noted by Wallace and Stead (1957). Stead and Kunkel (1939) found similar responses using paredrinol sulphate (a-N-dimethyl-p-hydroxyphenethylamine). Had a reflex mechanism been responsible for the venoconstriction, the SVP should have increased in every instance. The expected reflex adjustment would be venodilatation to counteract the increase in venous pressure which would increase the volume of blood centrally located in the heart and lungs. The SVP, in fact, decreased in three of the five experiments supporting a possible reflex mechanism attempting to compensate for the changes associated with the increase in venous pressure.

It is apparent, therefore, that noradrenalin acts not only on the arterial side of the vascular tree but also on the venous side. These influences on venomotor tone need further study in normal and abnormal cardiovascular states of both the pulmonary and the systemic circulation.

Procaine Block. Regional nerve blocks were preformed in 3 control subjects and five patients with CHF by injecting 3 to 10 cc of 2% procaine subcutaneously 2 to 4 inches proximal to the isolated venous segment. Care was taken to avoid anesthetizing the region where the PVP was being recorded. Figure 6 shows the mean response. Of the three control subjects, two had a decrease in venous tone of 80 and 140 mm H_2O, respectively, and one had an increase of 20 mm H_2O. Of the five patients with CHF, four had a decrease varying from 20 to 240 mm H_2O, and one had a rise of 65 mm H_2O. The period of observation varied from four to 14 minutes and the effect was usually obtained within five minutes. In the two instances in which there was an increase in venous pressure, the anesthesia was considered inadequate and the increase, a response to neurogenic and psychogenic stimulation. It is of interest that one subject showed a marked increase in SVP from 375 to 875 mm H_2O during the injection period followed by a decrease to 175 mm H_2O within four minutes after the injection was completed. The increase was attributed to neurogenic and psychogenic reflexes and the decrease to their interruption by the procaine. Following the regional field block the responses in general were diminished in magnitude, including the responses to neurogenic and psychogenic stimuli, liver pressure, application of a tourniquet proximally, and deep inspiration (Fig. 6).

The PVP did not change or increased 5 to 25 mm H_2O due to neuro-

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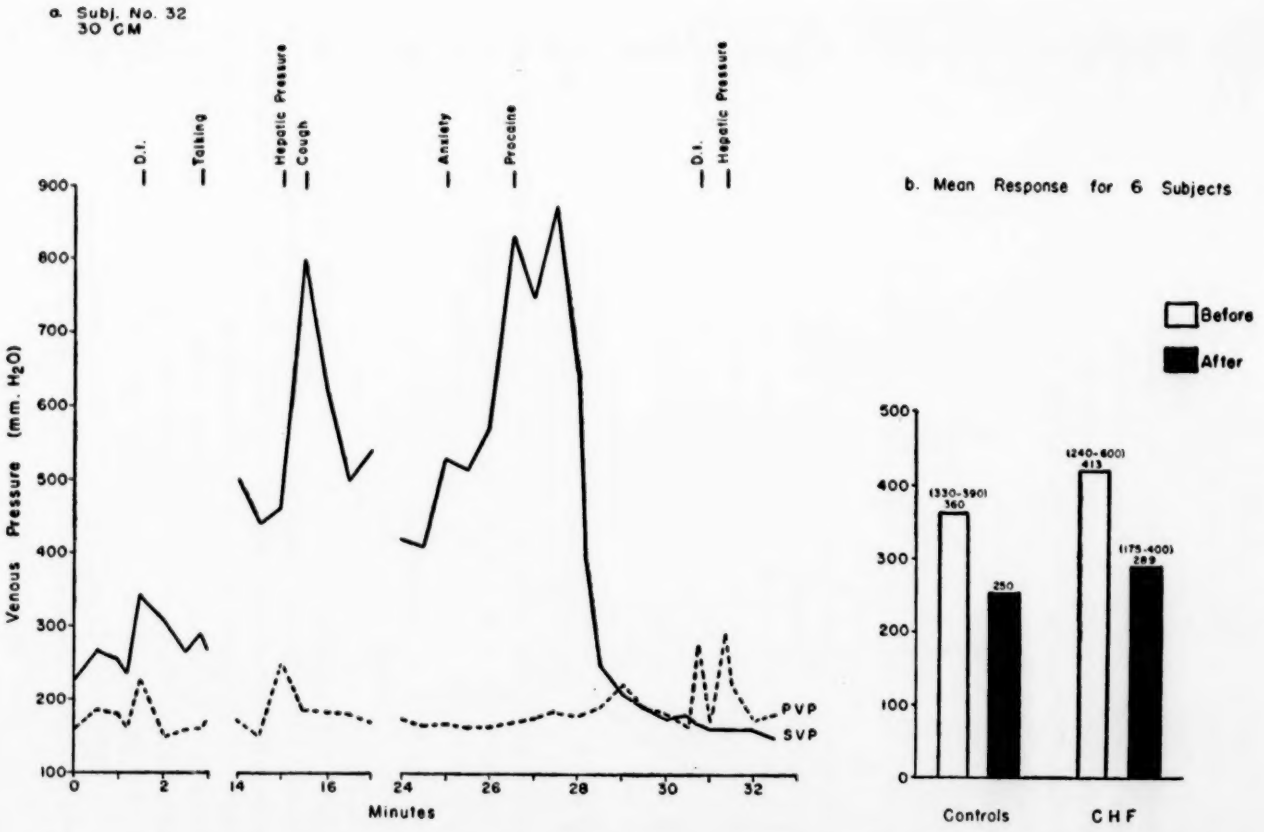

FIGURE 6. Illustration showing a decrease in segmental venous pressure (SVP) in the magnitude of the venoconstrictor response following deep inspiration and liver pressure after regional procaine block.

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genic and psychogenic influences over the period of observation except in one subject in whom a decrease of 20 mm H_2O was recorded.

In three control subjects stellate ganglion blocks * were made using 10 cc of 1% xylocaine. These were performed after a satisfactory baseline recording had been obtained. Complete Horner's syndromes were obtained in two subjects and a partial one in one subject. The effect on the SVP was variable. One subject with a classical Horner's syn-

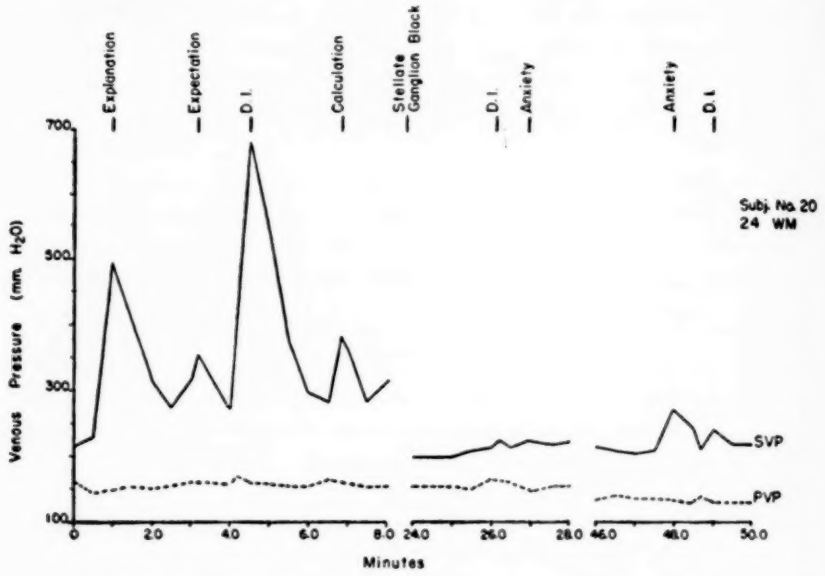

FIGURE 7. Illustration showing diminution in the magnitude of various reponses following stellate ganglion block.

drome had a steady rise in SVP and PVP. The second subject with complete Horner's syndrome had an increase in pressure during the process of blocking the ganglion but the SVP then decreased in 8.5 minutes to a plateau higher than the starting SVP. In all three subjects, however, the responses to stimuli such as deep inspiration, fear, anxiety and arithmetic problems were less after the ganglion block than before but the responses were not abolished (Fig. 7).

Duggan *et al.* (1953) also attempted stellate ganglion blocks in three subjects. In one subject they obtained an abolition of responses and

* The stellate ganglion blocks were done by Dr. T. E. Upton of the Anesthesia Department, Charity Hospital, New Orleans, Louisiana.

in the other two, in spite of the appearance of Horner's syndrome, significant venomotor responses persisted. Apparently all the sympathetic pathways to the venous segment were not interrupted by such a procedure. The increase in SVP in the two subjects in the present study might be explained by a partial stimulation of the stellate ganglion or by stimulation of other sympathetic pathways causing a reflex vasoconstriction as suggested by McDowell (1935) in his extensive review of the nervous control of blood vessels. It is likely that this represents the same phenomenon observed by Meyer and Middleton (1929) who noticed that venous pressure rose during the induction period of general anesthesia but as anesthesia became effective the venous pressure decreased to a plateau higher than the starting venous pressure. Nevertheless, the difference in response in SVP to the two types of procaine block is not clear. It is possible that during the regional blocking procaine seeped to the segment itself causing venorelaxation or it may be that the stellate ganglion block was incomplete. In either case the fact remains that the ability to respond to given stimuli was diminished following procaine blocking, partial or complete, of the sympathetic nerve fibers. This adds further support to the fact that venomotor tone is influenced by the sympathetic nervous system.

Deep Inspiration. The effect of a deep inspiration was recorded in 21 control subjects and seven patients with CHF with a total of 61 observations (Fig. 8). In all but three observations the SVP increased. In some subjects there was a slight decline followed by venoconstriction about two to five seconds after the onset of the inspiratory effort, reaching a maximum response after 15 seconds. In other subjects, primarily those with CHF, the venoconstrictor response was slower in onset and, once the maximum was reached, relaxation was gradual. In a few subjects, the venoconstrictor response began after the expiratory phase of respiration had already started—an unexplained delayed reaction. Apparently, the response of the veins in subjects with CHF was different from most of the control subjects. Wood *et al.* (1955) found a similar phenomenon in their studies. Following a systemic injection of hexamethonium and procaine block, the venoconstrictor response to deep inspiration was diminished in most subjects. As the effect of the above procedures disappeared, the normal response returned.

In some instances the deep inspiration was a Valsalva maneuver since the subjects held their breath once the maximum inspiratory effort was reached. The response was identical to that of a slow unheld deep inspira-

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tion. When the subjects fell asleep and suddenly awoke and inspired deeply the response was the same. For this reason all these maneuvers were considered to initiate similar reflex venomotor phenomena.

The PVP followed the expected reaction described previously.[4] On a maximum inspiratory effort for approximately 20 to 30 seconds there was an initial drop, usually less than 10 mm H_2O, almost invariably followed by a rise in venomotor tone. Six observations on four subjects, however, showed a lowering of the PVP, averaging 25.0 mm H_2O (range

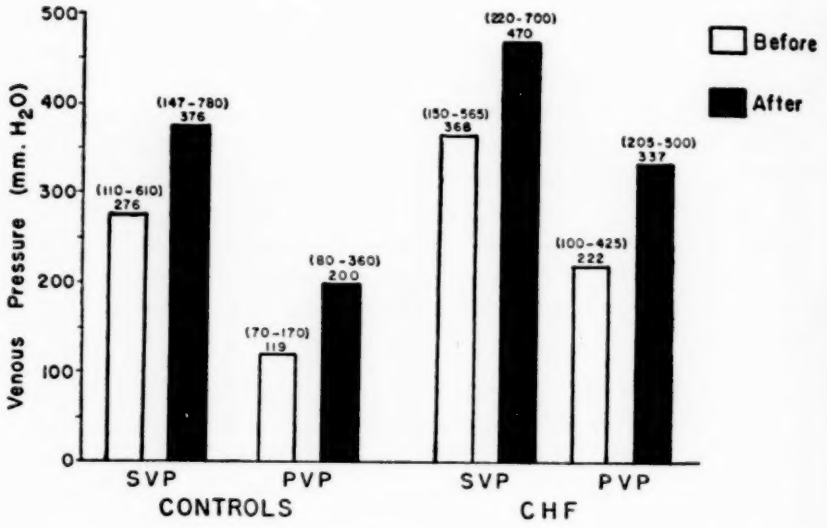

FIGURE 8. Changes in mean segmental (SVP) and peripheral venous pressure (PVP) produced by deep inspiration.

10 to 40 mm H_2O). The explanation might be that the subjects performed an abdominal rather than a thoracic type of deep inspiration.

The blood pressure also behaved as expected. There was a brief initial increase followed by a decrease and then an overshoot reaction for a few seconds when expiration ended. This has been described previously (Salisbury *et al.*, 1959).

The "habituation" or "tachyphylaxis" phenomenon described by Burch and Murtadha (1956) following successive deep breaths was different from that observed in this series. Six observations on four subjects showed a variety of responses from no change in one, to a

[4] Page, *et al.*, 1955; Bolton, *et al.*, 1936; Holt, 1943.

marked to slight increase in SVP in others and to a slight decrease in still another. In this group, however, the deep inspirations were taken in quick succession for a total of ten, whereas in the study by Burch and Murtahda they were repeated at a slower rate. This timing, as well as the respiratory performance of the subjects, is an important factor.

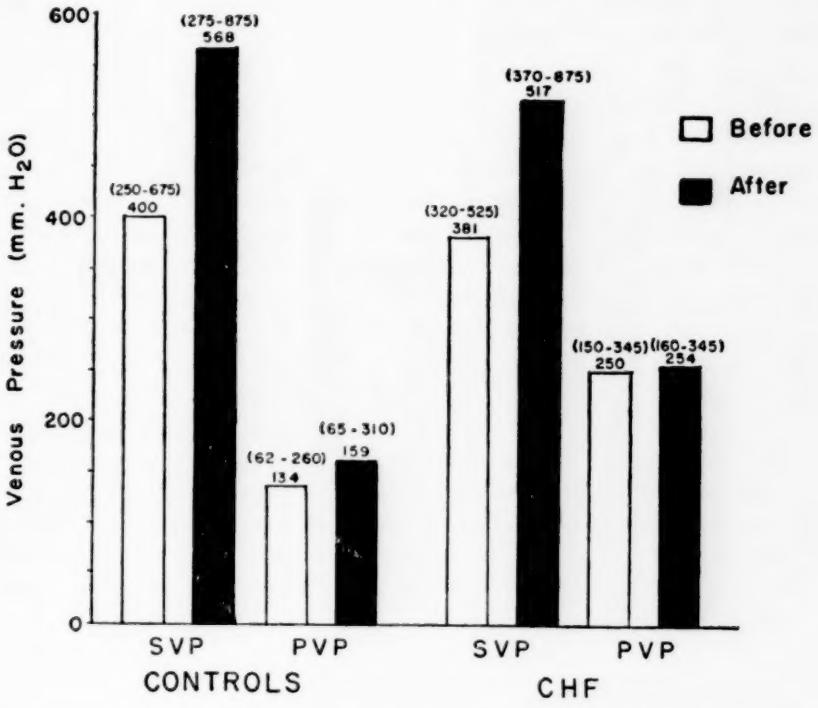

FIGURE 9. Effect of neurogenic stimulation, primarily pain, during venepuncture and stellate ganglion block on mean segmental venous pressure (SVP) and mean peripheral venous pressure (PVP).

A discussion of the possible reflex pathways that lead to the venoconstrictor response following deep inspiration has been discussed previously (Burch and Murtahda, 1956). Salisbury *et al.* (1959) experimenting with dogs showed that the blood pressure decreased when the lungs were inflated or stretched, although a constant blood flow was maintained by means of a heart-lung machine. From their illustrations it appeared that the PVP increased during the experiments. When the vagus nerves were blocked, the reflex disappeared. Similar responses

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had been previously noted (Page *et al.*, 1955; Meyer and Middleton, 1929). Page *et al.* (1955) also found that the PVP remained elevated longer than the SVP, whereas in these studies, the reverse was true.

Neurogenic Stimuli. The effect of pain produced by venepuncture or some other stimulus was recorded 16 times in 12 subjects, five of whom had CHF. In all experiments the SVP increased (Fig. 9). The magnitude of the rise in venomotor tone varied considerably with the type of

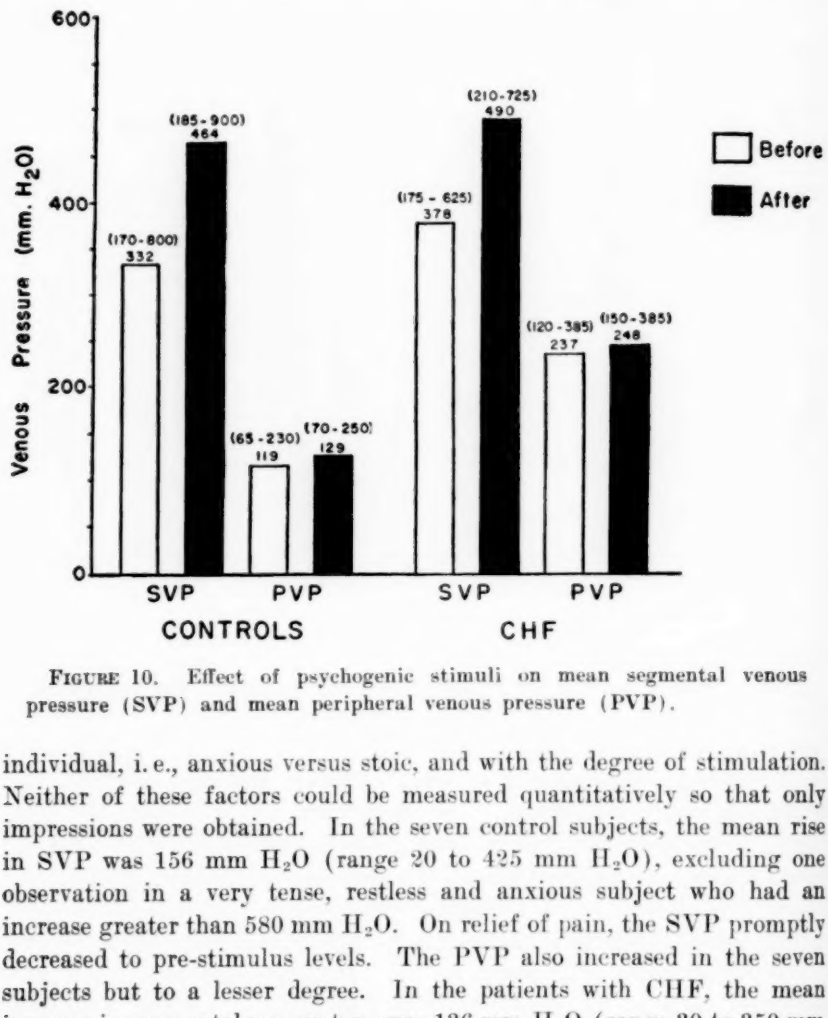

FIGURE 10. Effect of psychogenic stimuli on mean segmental venous pressure (SVP) and mean peripheral venous pressure (PVP).

individual, i.e., anxious versus stoic, and with the degree of stimulation. Neither of these factors could be measured quantitatively so that only impressions were obtained. In the seven control subjects, the mean rise in SVP was 156 mm H_2O (range 20 to 425 mm H_2O), excluding one observation in a very tense, restless and anxious subject who had an increase greater than 580 mm H_2O. On relief of pain, the SVP promptly decreased to pre-stimulus levels. The PVP also increased in the seven subjects but to a lesser degree. In the patients with CHF, the mean increase in segmental venous tone was 136 mm H_2O (range 30 to 350 mm

H_2O). This response, although not abolished, was certainly diminished by procaine block and the intravenous administration of hexamethonium.

Psychogenic Stimuli. The responses following psychogenic stimulation in association with anxiety, worry, fear, speaking and thinking were most interesting. Thirty-seven such tests were performed on 15 control subjects with an associated mean increase in SVP of 129 mm H_2O (range 15 to 400 mm H_2O) and 13 tests on six subjects with CHF with a mean rise of 112 mm H_2O (range 35 to 335 mm H_2O (Fig. 10). In both groups the PVP also increased by a mean of 10 and 12 mm H_2O, respectively. As expected, the individual variations were considerable depending on the degree of stimulation, the mental state and personality of the subject. For example, one subject was given three arithmetic problems to solve; namely, to subtract successively 7 from 100, 9 from 100, and 6 from 100. The first problem produced an increase of 100 mm H_2O, the second 130 mm H_2O and the third only 50 mm H_2O. The last response was probably low because the problem was easier or because the subject gained confidence in his abilities to handle the problems. The phenonmenon of "habituation" may also have been a factor. This phenomenon is little understood.

Most subjects were quiet and relaxed between experiments. The pressure tracings showed spontaneous variations without marked abrupt changes. As soon as a drug was prepared for use or a syringe unwrapped, however, venous tone began to increase until an acceptable explanation was given the subject or the source of disturbance removed. On several occasions the SVP and the PVP were noted to increase without apparent reason. These were assumed to be related at times to the subject's thoughts. When the subject became interested in the experiments and their results there was an increase in the SVP and sometimes in the PVP.

These responses apparently are mediated through the sympathetic nervous system. Local procaine blocking of the nerve pathways to the isolated segment partially or completely abolished the responses (*vide supra*). Because the segment itself might have been anesthesized by local blocking, thus making it less responsive to appropriate stimuli, stellate ganglion block was performed on three subjects as described above. In the two subjects in whom successful blockings were obtained, responses to psychogenic stimuli were diminished. In one subject (Fig. 7) mere approach with a hypodermic syringe and needle produced an increase in SVP but this was much less in magnitude than before the block. The responses to the same arithmetic problems were also much less after the block than before.

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That emotional factors can influence CHF has been discussed by Chambers and Reiser (1953). They studied 25 consecutive subjects with CHF and found significant emotional stress to be present just before the onset of heart failure. The influence of psychogenic stimuli has been studied by Burch and Ray (1948) and Martin and associates (1959). In both studies responses similar to those described here were found. Martin and associates only studied normal subjects and raised the question whether or not the veins of subjects with CHF could respond similarly to appropriate stimuli. It is evident from the present study that they do respond and constrict further on psychogenic stimulation.

It is apparent, therefore, that psychogenic stimuli can have a marked influence on venomotor tone. Considering the magnitude of the changes, it is easy to imagine the magnitude of the venomotor responses which might follow a sudden emotional upheaval. Such a generalized constriction might so increase the venous return to the heart and congestion in the vessels of the lungs that, together with the changes occurring in the arterial side of the circulation, an acute cardiac catastrophe could easily result. This probably explains in part why so many patients develop acute pulmonary edema or acute CHF following an acute emotional disturbance.

Digitalis. Two subjects with acute congestive heart failure and one with early CHF without previous therapy were rapidly digitalized by intravenous administration of lanatoside C. Two received 1.6 mg of the drug and the third received only 1.2 mg because premature beats developed and the drug was temporarily discontinued. Venous pressure was recorded from 20 minutes to two hours after completion of the injection. During that period of observation no particular effect was noted on either the SVP or PVP. The response to deep inspiration, anxiety and pain remained unchanged. That the digitalis had an effect on the cardiovascular system was evident later in the day when diuresis ensued; the heart rate slowed and there was general clinical improvement in the patient's health.

Braun and Fryd (1951), while studying the effect of priscol on venous pressure, referred to three subjects who were given digitoxin. They found a decrease in the venous pressure following digitalization in two of the subjects and no change in one. It is not clear, however, whether or not this change in venous pressure occurred within a few hours after digitalization or several days later.

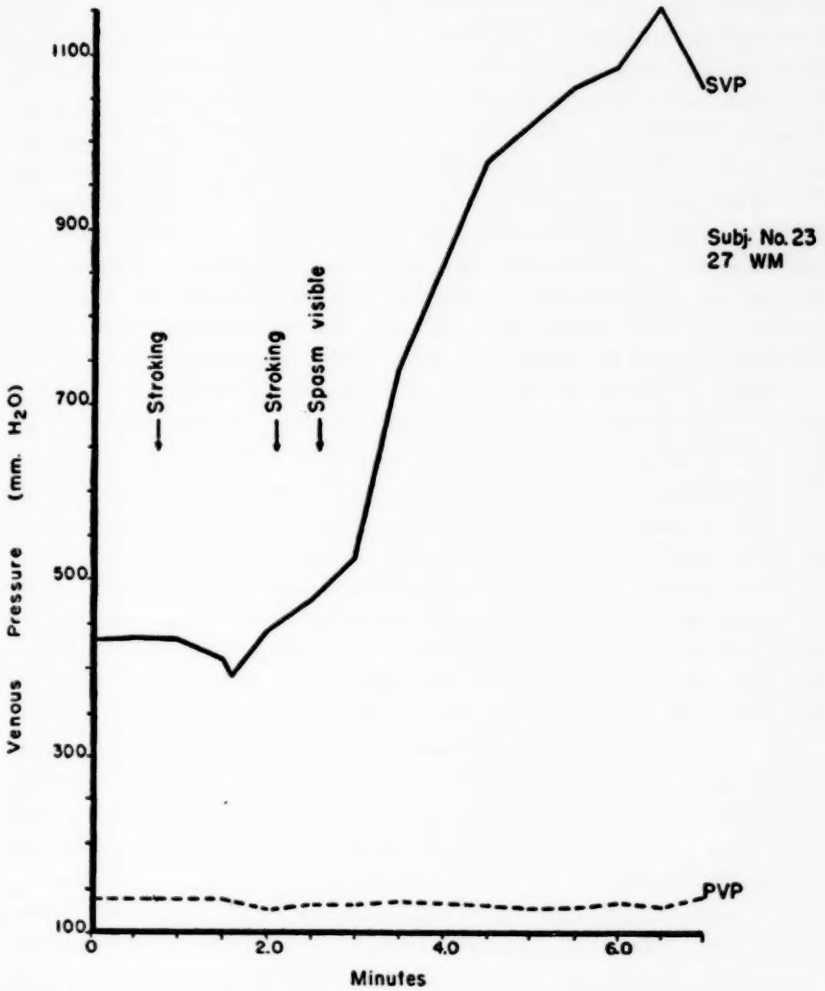

FIGURE 11. Influence of venospasm on segmental venous pressure (SVP). Note the decrease in SVP while stroking the skin over the isolated venous segment the first time. The second time the skin was stroked spasm developed probably as a result of injury to the wall of the vein in the regions of the needle tip.

Venous Spasm. It has been demonstrated that veins have intrinsic venomotor tone and rhythmicity (McDowell, 1935; Franklin, 1925; Folkow, 1955). This independent behavior is further supported by observing the development and subsidence of localized venous spasm.

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In several subjects ring-like spastic contractions developed either spontaneously or following stimulation during stroking the overlying skin. When this occurred, either the SVP rose markedly (Fig. 11) or the tracing became a straight horizontal line with the disappearance of spontaneous variations in pressure. Examination of the venous segment usually demonstrated dilatation distal and proximal to the spastic ring. Whenever this occurred no further tests were possible until the spasm subsided, which was usually within a few minutes. In a few instances, however, it failed to subside and the experiments were discontinued. The development of such a spasm was considered to represent accidental injury to the wall of the vein by pressing the wall between the glass rod over the skin and the needle in the lumen of the vein.

It was of further interest to note that occasionally the spasm following trauma involved the whole isolated segment. In at least two instances the spasm was such that after removal of the occluding wedges and needle and after the application of a tourniquet to the arm proximally, the area of spasm stood out prominently as an empty segment of vein and felt cord-like on palpation. Attempts to force blood through the spastic segment were usually grossly unsuccessful. Local procaine infiltration failed to relieve the spasm. After a variable period of time, the spasm subsided and the vein appeared completely normal. It was felt, however, that local factors had not returned completely to normal, for attempts to perform a venepuncture in the same area often led to further spasm necessitating the discontinuation of the experiments or the isolation of a new segment elsewhere in the forearm. Similar experiences have been described previously (Burch and Murtadha, 1956). Such behavior of a small venous segment supports the presence of active local factors which influence venemotor tone.

GENERAL DISCUSSION

From the foregoing experiments it becomes evident that the forearm veins of man are extremely active. It is apparent that they react to a variety of physical, chemical, neurogenic and psychologic stimuli and that the reactions can be of considerable magnitude. It must be remembered, however, that the magnitude of the changes in venous tone varied considerably with the psychic state of the subject, his personality, mental state and the magnitude of the stimulus. Also, the changes in pressure noted in the isolated segment were magnified by the nature of the preparation, that is, a closed cylindrical compartment filled with noncompressible liquid.

The smaller changes noted in the open peripheral vein also become very important when the size of the venous compartment is considered. A small change in venous tone throughout the whole venous compartment can produce a sizable shift in blood either out of or into the venous bed. As pointed out by Guyton *et al.* (1955) sizable increases in arterial resistance cause but a small drop in cardiac output, whereas the same change in venous resistance in the large veins produces a marked decrease in cardiac output. Rashkind *et al.* (1953) also concluded from their experiments on dogs that changes in the venous return to the heart were controlled to a large extent by the postarteriolar vessels, most likely the veins. They considered coordinated arteriomotor and venomotor behavior responsible for vascular adjustments. This would be in agreement with the findings of Alexander (1954) in his experiments with the mesenteric vessels of dogs although he also felt that the two mechanisms sometimes worked independently. Recent studies from this laboratory also support this concept for the small vessels in the tissues (Burch, 1959; Burch, in press). Landis *et al.* (1950) also postulated that venomotor and arteriomotor reflexes occurred together, but usually in the same direction. This apparently is not always true (Duggan *et al.*, 1953; Burch, in press; Burch, to be published). That the changes in the peripheral veins often reflect the change in the central larger veins was shown by Gauer and Sieker (1956). They measured the venous pressure in the superior vena cava and in the veins in the antecubital fossa and found that the changes were in the same directions in both although the pressure was higher in the smaller peripheral veins. The finding that the venous pressure increases from larger to smaller veins has been previously reported and is confirmed by the observations of the present study.[5]

That veins can act independently of the other vessels is suggested from several experiments. Franklin (1925) found intrinsic rhythmic movement in mesenteric rings of vein of sheep. In another paper (1928) he quoted Gubler as saying that veins respond to tapping by constriction followed by localized dilatation. Halmagyi *et al.* (1952) indicated that the increase in venous pressure in congestive heart failure was probably due to a neurogenic factor as well as to a mechanical factor. Landis *et al.* (1950) added that with an increase in blood volume in pregnancy there is no, or a slight, increase in venous pressure and that without an increase in blood volume in congestive heart failure there can be a marked

[5] See Burch, 1954b; Oschner, *et al.*, 1951; Wallace and Stead, 1957; Winsor and Burch, 1946.

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increase in venous tone. Both types of patients often have apparently normal arterial blood pressures thus eliminating arterial constriction. Hooker (1921), in his extensive review of the subject, cited evidence to support the individuality of venomotor tone under some circumstances. Alexander (1954), as stated above, found independence of arteriomotor and venomotor mechanisms. McDowell (1935) found the return of vasomotor tone following sympathectomy indicative of an intrinsic mechanism for the regulation of vascular tone.

In the present study a few salient facts are worth noting. The application of the occluding wedges sometimes led to apparent spasm of the isolated venous segment. In fact, such localized spasms developed following venepuncture indicating an independent local behavior of the vein under study. Trauma associated with stroking also caused the same phenomenon in some instances. In time, the spasm would always subside. Gentle stroking of the skin without trauma to the wall of the vein resulted in venodilatation, a well established observation.

The ganglionic blocking agents led to a marked decrease in venous tone and clinical improvement in the subjects with congestive heart failure.[6] Using hexamethonium, the same results were obtained in this study. The effect of the agents, in the doses used, on arterial blood pressure and pulse rate was minimal. Thus, these drugs appear to be helpful adjuncts in the treatment of congestive heart failure when venous tone is high. The influence of the drug on the arterial blood pressure subsided more quickly than the decrease in tone produced in the veins.

The infusion of noradrenalin led to the expected rise in PVP and blood pressure and to the slowing of heart rate. The changes in the SVP, however, are not clear. The decrease in SVP in three out of five instances may be a reflection of a compensatory reflex phenomenon in an attempt to overcome the increase in venous pressure and, hence, in venous return to the heart and lungs. This requires further study.

Local procaine block and stellate ganglion block resulted in a diminution in the responses of the isolated segment, but not all responses were abolished or diminished. In one instance both the PVP and the SVP continued to increase despite the appearance of a Horner's syndrome in the subject. It is possible that sympathetic pathways to the venous segment other than those through the stellate ganglion exist. This is discussed by Folkow (1955). This observation needs further study.

[6] As has been previously described by Burch and Murtahda, 1956; Duggan, *et al.*, 1953; Burch, 1954a, 1956; Kelley, *et al.*, 1953; Shuman, 1950.

The responses observed during deep inspiration and Valsalva maneuvers have been extensively discussed by other investigators as quoted by Burch and Murtadha (1956). Suffice it to say that the present observations concur with those described previously.

The importance of the responses to psychogenic stimuli cannot be overemphasized and their relation to congestive heart failure deserves further study. The responses to apprehension were observed fortuitously by Page and associates (1955). Ackner (1956), discussing digital plethysmography, emphasized the changes observed with emotional stimuli and with the degree of alertness of the subject. The relation of emotional stress to the precipitation of congestive heart failure has already been mentioned (Chambers and Reiser, 1953).

In conclusion, it is evident that variations in venous tone play a very active part in the regulation of the circulation both in health and in disease. Further study is needed to elucidate the many factors involved as well as to explain the changes observed. In particular, the effects of psychogenic stimuli must be adequately studied.

SUMMARY

1. Thirty-five subjects, 11 with and 24 without congestive heart failure, were studied with the isolated venous segment technique. A separate peripheral vein to the systemic circulation was studied concurrently.

2. The effects on venous tone of stroking the overlying skin, hexamethonium, noradrenalin, local procaine field block, stellate ganglion block, digitalis, deep inspiration and Valsalva maneuvers were studied and described.

3. The venomotor responses to neurogenic and psychogenic stimuli were studied and marked increases in venomotor tone were found.

4. It is suggested that hexamethonium and other sympathetic ganglion blocking agents may be useful adjuncts in the treatment of congestive heart failure when venous tone is elevated.

5. It is sugegsted that the mechanisms regulating venous tone probably play an important part in cardiovascular adjustments in health and disease.

6. The phenomenon of local venospasm is described.

7. There is a need for additional studies of the mechanisms regulating venomotor tone.

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A TEST OF PREDICTIONS BASED ON CAUSAL HYPOTHESES

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THE observational study, in which experimental control and randomization are absent, is never subject to a simple, unchallenged interpretation. Nevertheless, the observational study is necessary; for it is seldom possible to perform randomized experiments in populations of ultimate interest. This is so particularly in the study of man. While genetic traits may be in part the result of random forces, we can not randomize race or age to individuals, or socio-economic status, religion, place of birth, social customs, and so forth. Granted that certain volunteer groups can sometimes be obtained for the experimental trial of therapeutic agents, or of some other kind of treatment, these groups are not the population of ultimate interest. The conditions under which demonstration of a causal relation, through controlled experimentation, is feasible are usually not the conditions under which we seek to establish, ultimately, a causal relation. Consequently, even those experiments among volunteer or selected groups must be bolstered by observational studies of the population.

Some observational studies are initial explorations. The existence of a problem is the initiating force, and the purpose of this kind of study may be merely to uncover some relationships which suggest causal mechanisms. Other observational studies can be taken up to test hypotheses arising from experimentation, from previous observation, or from both. More generally, observational studies can serve both the purposes of exploration and of hypothesis testing. (There may be, of course, other purposes with which we are not directly concerned in this paper).

Exploratory methods of analysis are much more "free-wheeling" than those suited to hypothesis testing. In searching for observed relationships one may classify and re-classify the data in any number of ways he may choose. But any relationships thus found are quite inconclusive; neither statistical nor practical significance can be attached to them. They may constitute, nevertheless, valuable bases for hypotheses which should be tested in further studies. This is the potential value of exploratory study: to help develop hypotheses for future testing.

The hypotheses which should be tested in future studies must be pre-formulated. By the same token, hypotheses tested in current studies should have been pre-formulated.

Now the pre-formulation of hypotheses, with a view to testing them against observational data, is often neglected. It is true that in the planning stage of the study, some broad hypotheses may be stated. But these are often of the simple form: "the hypothesis is that factor X is associated with factor Y." It is not hypothesized what the level of association should be, or under what circumstances the level of association will vary, or what causal framework is involved, or what factors require adjustment before measuring the associations. Only the direction of association is predicted.

If all the adjustments (such as age, sex, race, social class, etc.) to be made are specified, this is likely to be done merely because adjustment for them is customary rather than because such adjustments are related to a specified causal framework. After such vague formulation of hypotheses, there is little that can really be tested.

This paper is not devoted to prescribing how one should arrive at an hypothesis. That is a mysterious process. Certainly prior research and information of an historical nature is involved in the development. In general, when enough background material is available, relative values of dependent variables can be predicted at levels consistent with past observation (although the predictions may often be erroneous). And it seems reasonable that these levels should also be consistent with any causal hypothesis which might be developed, since, in general, the causal hypotheses should agree well with known past observation. But also the ability of an investigator to form simplifying concepts to explain phenomena, through analogy, generalization or whatever imaginative device, is also strongly involved.

Again we say that we are not prescribing how an hypothesis should be developed. No matter how it comes about, what we wish to do is to test the hypothesis, once a suitable prediction based on it has been formed, against observed data.

If, as we have implied, a prediction of some sort, based on a causal hypothesis, is desired in order to test an hypothesis, then it seems reasonable to say that the more that is predicted, and the more specific the prediction becomes, the more can be put to test in the observational study. Merely to predict that X will be positively associated with Y, after adjusting for $Z_1, Z_2, \cdots, Z_m$, for example, provides little to test. But to add that the level of the adjusted association should vary according

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to a specified pattern under a variety of different specified circumstances would provide a great deal more to test.

We recognize, however, that there are limits on the value of increasing the number of circumstances under which variations in degree of association are specifically predicted. Perhaps there is no causal framework, or not even a natural law, which is sufficiently general and sufficiently detailed to permit accurate predictions under an unlimited number of different circumstances. That is, it may be that every causal framework would be shown wanting, at least in some detail, if tested under an unlimited variety of circumstances.

This leads us to an unresolved problem as to where to strike a balance between predicting practically nothing and predicting practically everything. In this paper we set down four general criteria for a test of a prediction. These are not the only criteria which could be stated, and there may indeed be better ones in some sense. What we wish to do, however, is to point out that these criteria would provide a fairly stringent test of a causal hypothesis. A causal interpretation carries much more force if such a test is met than if practically no test at all is made.

THE FOUR TEST CRITERIA

We have already discussed the importance of making a prediction, reasonably specific, pertaining to a variety of circumstances, and arising from a causal framework. In order to test such a prediction against observed data, the variety of circumstances under which different effects are predicted must, of course, be available for study. When the observations have been taken then, both a predicted pattern of variation and an observed pattern of variation in the level of effects under the varying circumstances will be available. The test will then involve a judgment as to whether the prediction is correct. Experience tells us that perfection in the prediction, even in the best of situations, is quite improbable. There will be some disagreement between prediction and observation, as a rule. Experience also tells use it is not necessary that a causal hypothesis give rise to perfect predictions in order to be useful. But it is a problem to decide just what should constitute a successful prediction. Where do we draw the line between success and failure?

Many more or less arbitrary solutions to this problem could probably be set down. Some of them would depend on knowledge or assumptions about the particular subject in a given study. We would rule these out of contention as acceptable general tests, for the criteria would vary in

kind from one study to the next. Other solutions might be purely arbitrary, supported by no rationale, and we would rule these out.

The proposed test we have chosen to present here is one of the many possible. It is frankly open to controversy and it does have some arbitrary features. But it does also appear to satisfy our requirements that it be of general applicability and that it be supported by some rationale. It is expressible in two parts:

to be a successful prediction,

(a) the prediction should account for a statistically significant amount of variation in effects;

and (b) the residual variation, after removal of variation predicted on the basis of the causal hypothesis, should be low enough to be assigned to chance fluctuation; that is, residual variation should not be significantly large.

The very statement of these two related criteria implies that the causal hypothesis must be of a special form. Firstly, the requirement that a significant amount of variation be taken up in the prediction implies that the causal hypothesis must have been sufficiently developed that it anticipates *some* (not necessarily all) circumstances under which effects will differ. Secondly, and just as important, the requirement that residual variation be not significantly large implies that the causal hypothesis should take into explicit account enough conditioning factors so that variations in observations, due to innumerable other factors, will appear to be approximately random.

These are indeed strong requirements. Accordingly it is our belief that the causal hypothesis which leads to a 'successful' prediction earns a degree of credence.

These criteria also imply that the prediction itself be of such a form that observed variation in effects can be separated into two (additive) components. The first component is that which is taken up by the prediction; this can be referred to as the agreement component. The second, residual, component can be referred to as the disagreement component.

The form of the prediction, which we shall illustrate, is an index. For example, if a prediction is to be made about an effect under m different circumstances, Z_α, the prediction will be in the form of a set of numbers, C_α, $\alpha = 1, \cdots, m$. If we denote the 'true' level of an effect by E_α, then we take C_α to be linearly related to E_α as follows:

$$E_\alpha = a_1 + a_2 C_\alpha,$$

where a_1 and a_2 are some unknown constants.

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Thus, it is not required that the prediction index correspond in level or scale (a_1 and a_2) with observed effects. What is required is that the prediction, C_α, be significantly correlated with observed effects, and this correlation is required to be linear.

This linearity requirement appears at first glance to be quite arbitrary. But, in fact, it does not impose any strong limitations on the practical applicability of the test. This is because of the freedom which the investigator has both in specifying the prediction index, C_α, and in choosing the units of measurement. He is free to choose any set of values of C_α; they need not form an arithmetic, geometric, or any other familiar type of sequence. Further, he is free to choose whatever units of measurement or transformation of variables which may be relevant in defining effects. In view of this freedom, it is necessary that *some* type of relationship between the index and the 'true' effects be pre-specified. Without some pre-specified relation, the so-called prediction would degenerate into no prediction at all. We require that the investigator choose the prediction index and the units of measurement which permit an analysis based on a *linear* model. The reason for setting the linearity requirement, rather than some other requirement, is that the analysis is thereby made relatively simple.

Finally, a word on the choice of index values, C_α, is in order. Despite the fact that the C_α values need not accurately reflect the level or scale of predicted associations, the requirement that they correlate significantly with observed associations is a strong one. This being so, the investigator might sometimes feel that to specify a single set of C_α values would be too arbitrary. If this were the case, and in practice it might often be the case, it would be indicative that the causal hypothesis was not sufficiently developed to provide very specific predictions. At the same time, it should motivate the investigator to review previous work in the same area in order to obtain data which could be used to help in specifications of the index. If such prior data were not available, this would still not rule out making a test. Theoretically, a region containing all those sets of C_α concordant with the causal hypothesis could be specified. If any one of the concordant sets of C_α failed to meet the test, according to the criteria we have set, the prediction would be unsuccessful, or rather, not completely successful. If it were partially successful, *i.e.*, some but not all concordant sets of C_α were successful predictions, then this would possibly spur the investigator to formulate a more restricted set of concordant C_α values for test in a future study. In this way we see that the designation of regions of concordant C_α sets would not be entirely free of

'exploratory' aspects. However, in this paper, we shall restrict our attention to an illustration of the test of a single, although admittedly a somewhat arbitrary, set of C_α values.

To summarize, the four test criteria are:

a) a fairly large number of varying conditions should be available for analysis, giving effects an opportunity to manifest themselves in various ways;

b) a prediction (index) of variation under the varying conditions should be specified;

c) the prediction should account for a significant amount of variation (significant agreement, based on linear model);

d) the residual unpredicted variation should not be significantly large (insignificant disagreement, linear model).

Failure to meet any one of these four criteria would, we believe, be unfavorable to the causal hypothesis in its stated form.

This proposed test of a prediction is not intended to 'prove' or 'disprove' causation. As stated before, a causal interpretation of uncontrolled data seldom, if ever, can go unchallenged. Important subjective considerations are involved in the general acceptance or rejection of the causal hypothesis. Rather the proposed test is intended as a rigorous trial of causal hypotheses. It is believed that the great majority of such causal hypotheses would fail to meet the test in some way, and in so failing, the directions of future research might be more clearly indicated. In the event that the test were met, on the other hand, the causal hypothesis would be substantiated, but, of course, not proven to be irrevocably true. The future course of action indicated in this event would to test the same hypothesis again with new data under different circumstances.

ILLUSTRATION: A TEST OF NON-COMMUNICABLE HEALTH PROBLEMS AS CAUSE FOR SUBSEQUENT HEALTH PROBLEMS IN THE HOUSEHOLD

Few persons will contest that some diseases "run in households." Communicable disease is a notable example: it is reasonable to believe that transmission of a biological agent of disease from one household member to another, in general, is more easily accomplished than direct transmission to persons outside the household. It is also granted that some hereditary diseases, such as diabetes, may tend to cluster in households. In addition, poor housing conditions and other environmental

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stresses common to all members may be responsible for the clustering of health problems in households. Again, the psychiatrist may relate the development of mental illness to household tensions. Further, "accident-prone" persons, those who have "too many" accidents, may very well cause injury to others in the household. And, finally, it may be that chronic disease in one member sometimes induces tensions among other members, leading to diseases of varied kind. All these examples of possible familial aggregation illustrate the generally held idea that illness of one member of a household implies an increased tendency for illness in the other members.

In view of this generally held idea, it would seem natural to inquire whether non-communicable illness itself causes subsequent illness in initially healthy members of the household; this is the germ of a causal hypothesis.

To develop this hypothesis, we may conceive of it as a "stress" hypothesis. It may be reasoned that the stress of non-communicable health problems causes an alteration of some kind in the lives of the healthy members of the household. This alteration in activities and responses may or may not result in a health problem for a given person. By reason of the stress, some persons may escape a health problem, while others may acquire one, while still others may escape one problem and acquire another, and the health problem status of still others may be completely unaffected by the stress. Evidently, the mechanism of response would be manifold and it would be quite impossible to specify any single mechanism operating in the general population. Nevertheless, it should be possible to make a prediction of those circumstances under which a greater or smaller average response could be expected, concordant with the stress hypothesis. (Actually, as we have indicated before, a whole region of such predictions might be formed, because of the imprecision of the hypothesis, or because of the lack of data from past experience which would furnish a guide to making a single prediction. But for illustrative purposes, we shall develop a single, although somewhat arbitrary, prediction for testing).

Now, before a specific prediction can be made about the responses to health problem stress, we shall first have to define our terms: what is a household, when is a person considered to have a health problem, upon what persons in the household is the stress presumed to act, and what measure shall be used to indicate response to the stress. Furthermore, in order that a specific prediction, once formed, be tested, it is necessary that the definitions be applicable to data. Thus, it is necessary to

know the circumstances under which the data will be, are being, or were collected. (Actually, the survey data which we use in this illustration were collected for "exploratory" purposes some years ago. It is important that the "prediction" be made independently of any knowledge other than the conditions under which the data were gathered, and we do this here. Ideally, the prediction would precede the actual collection of data, not only to insure that the prediction be formed independently, but also to permit the prediction to dictate, in part, the survey design. In the present illustration the reverse is true; the survey design has in part dictated the scope of predictions which could be made).

Let us therefore describe the sampling design and define the terms which pertain to our particular illustration.

Source and Limitation of the Data

The material for this study comes from a survey of a district of Pittsburgh, Pennsylvania. In July 1951, the Graduate School of Public Health, University of Pittsburgh, conducted a survey of some 3,000 households in the central portion of the Arsenal Health District of the Pittsburgh Health Department. The area sampled by the survey comprised 22 of the 194 census tracts in the city and had a total population of about 80,000. On the basis of average monthly rental data, households in the study area were judged to be well below the rest of the city in income level. One of the principal objectives of the study was to measure the health characteristics of households in the area by means of personal interview of responsible members of the selected households.

A detailed discussion of the sampling design is given by Horvitz (1952). Some of the main features are described below. The 468 blocks in the district were classified into three strata, according to the number of dwelling units occupied (1,940): Stratum I, 100 or more; Stratum II, 50 and less than 100; Stratum III, less than 50. The primary sampling unit within each stratum was the block. For each selected block a proportion of the dwelling units in that block was chosen for interview. The block sampling ratios and dwelling unit sampling ratios within a given block were so chosen that each dwelling unit in the entire study area had an equal chance (approx. 2/15) of entering the sample. Both blocks and dwelling units within blocks were selected by systematic sampling with a random start; the analysis, however, treats dwelling units as randomly selected elements within strata. In June 1952, approximately one year later, the same households as were selected in

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1951 were interviewed again, unless the household had moved or refused to cooperate in the second survey.

The response problem was given particular attention in the design of the first interview. From a study of illness rates in relation to various interviewer groups, Horvitz concludes there were differences in illness rates elicited by the various interviewers. (Consequently, our analysis adjusts for certain interviewer characteristics as well as for sample strata.)

TABLE 1

An account of non-respondent and excluded households

Total Households Initially Selected for Interview:			2957
Less: Failed to cooperate, 1st Interview—		166	
Non-respondent, 2nd Interview—			
Failed to cooperate	220		
Moved away	251	471	
Total Non-response, Either Interview:			637
Households for which Some Data Available from Both Surveys:			2320
Less: Information Incomplete for One or More Members—			49
Households for which Complete Data Available form Both Surveys:			2271
Less Exclusions:			
No Members Free of Health Problem in 1st Year—	58		
Communicable Disease Present at 1st Interview—	71		
Total Exclusions.			129
Total Households Available for Analysis:			2142

One important limitation of the data, as for most survey data, is non-response. Table 1 shows that, of 2,957 households initially selected for interview, 166 failed to cooperate in the first interview; another 220 which cooperated in the first failed to do so in the second. An additional 251 households moved after first interview and were lost from observation. For 49 of the remaining households, information on one or more members is incomplete. This leaves 2,271 households for which complete information is available from both surveys. Of these, there are 58 in which no members were free of health problems as of the first interview. An additional 71 households are excluded from the analysis because communicable disease was present at first interview. Thus, we are left with 2,142 of an original 2,957 selected households. In a strict statistical sense, then, the results of this study are not generalized to include those households in the community,

(a) which would not have cooperated,

(b) which would have moved,

(c) which would have failed to give certain pertinent information,

(d) which would have no members initially free of health problems, or

(e) which would have reported a communicable disease at the first interview.

It is noted, however, that communicable disease in the second year is not excluded as a sequel to non-communicable health stress in the first.

A further limitation of the data is that their accuracy is limited to the accuracy of respondents' recall.

Definitions

As indicated before, in order to analyze the problem in specific terms, certain measures must be defined. They must be unambiguously applicable within the limits of the survey. Furthermore, they must be in accord with both the causal orientation and the prediction which is to be tested. Thus, the definitions tend to fix the causal hypothesis and the concordant prediction, *ad hoc.*

(1) A household consists of a number of persons living at a common dwelling unit. In the great majority of cases, the household is equivalent to a family, or a single person living alone, but there are a few cases for which more than one family, or several unrelated persons constitute a household.

(2) A person with a health problem is:

one with a reported physical impairment or chronic disease existing within one year prior to interview;

one reported hospitalized at any time in the year prior to interview, except hospitalization for delivery without complications, and except for routine check-up;

or, one reported to be semi-ambulatory or confined to bed for any interval during the month prior to interview. This definition is made in view of the limitations of the survey. It was felt that respondents could not give accurate histories of illness beyond one month prior to interview, except for hospitalization and chronic illness. This definition of a person with a health problem conforms closely to that adopted in earlier studies based on the Arsenal Survey. (Ciocco *et al.*, 1953)

(3) A person with a communicable disease is any reported person

with a health problem, who, in the month prior to interview, had an illness coded (International Statistical Classification of Diseases, Injuries and Causes of Death, 6th Revision, 1948):

001-138 infective and parasitic,
470-475 acute upper respiratory infection,
480-483 influenza,
490-493 pneumonia.

(4) The age of a person is taken as the reported age in years to last birthday prior to first interview.

(5) A propositus is a reported person, over one year of age at first interview, who had no health problem during the first year, and who did not leave the household in the second year, except by reason of death or illness.

(6) A propositus household consists of all the propositi in the household.

The Effect

The measure of relation between prior and subsequent household health problems can, for the sake of brevity, be termed the serial relation. The serial relation is defined in terms of the four-fold table represented as follows:

Four-fold classification of propositus households according to household health status at first interview and propositus household health status at second interview, in the αth sample category

FIRST INTERVIEW	SECOND INTERVIEW: No health problem in propositus household	SECOND INTERVIEW: Health problem in propositus household	TOTAL NUMBER OF HOUSEHOLDS
No household health problem	$n_{11\alpha}$	$n_{12\alpha}$	$n_{1.\alpha}$
Household health problem	$n_{21\alpha}$	$n_{22\alpha}$	$n_{2.\alpha}$
Total number of households	$n_{.1\alpha}$	$n_{.2\alpha}$	n_{α}

Let $p_{1\alpha} = n_{12\alpha}/n_{1.\alpha}$ and $p_{2\alpha} = n_{22\alpha}/n_{2.\alpha}$;

also let $p_\alpha = n_{.2\alpha}/n_\alpha$; $q_\alpha = 1 - p_\alpha$, and $p'_\alpha = n_{2.\alpha}/n_\alpha$; $q'_\alpha = 1 - p'_\alpha$.

Then the measure of relation which we have in mind is,

$$r_\alpha = (p_{2\alpha} - p_{1\alpha}) \sqrt{p'_\alpha q'_\alpha / p_\alpha q_\alpha}.$$

This is easily shown to be equal to the product-moment correlation. But in the form presented above, it is clear that the product-moment correlation for the 2×2 table is interpreted as an adjusted effect: it is a difference between two proportions, $p_{2\alpha}$ and $p_{1\alpha}$, adjusted for inherent variability in the proportions due to differences in the size of the first interview status categories (adjustment factor $\sqrt{p'_\alpha q'_\alpha}$), and adjusted for variability due to the average level of the proportions (adjustment factor $\sqrt{p_\alpha q_\alpha}$). Thus, the adopted measure of relation is a standard difference in second year household health problem rates. This is a comparison for households with and without first year health problems. We take this, r_α, as the observed effect, of which the pattern of variation is to be predicted.

In the above definition, r_α is the simple product-moment correlation between first and second year health problem status in the α^{th} sample category. More generally, r_α can be the partial correlation between first and second year health problem status in the α^{th} sample category, after adjusting by least-squares technique for the effects of a number of conditioning variables within the α^{th} category. In the present instance, the categories, α, into which the sample is divided will be based on size of propositus household, average age of propositus household, and sex distribution of the propositus household. Within each of these size-age-sex specific groups of household, the serial relation, r_α, is determined after adjusting by least-squares for the main effects of interviewer characteristics and of sample strata. (This adjustment procedure is carried out on the IBM 650 computer. Details of this technique are not presented here because they are of no importance to the principal purpose of this paper).

The Prediction

Now that specific terms have been defined, we may return to the elaboration of the causal hypothesis as it applies to making the prediction.

In accord with the idea of stress, it seems reasonable to hypothesize that the stress of first year health problems should be greater if borne

by a single propositus (healthy person in the household in first year) than if borne by more than one propositus. Therefore, let it be hypothesized that, other things being equal,[1] the serial relation should increase in a positive direction as propositus household size decreases. Thus, propositus household size will be one factor of the varying circumstances under which the pattern of effects (serial relations) is to be predicted.

Again in accord with the idea of stress, it might be true that younger propositi are more flexible in reacting to a non-communicable household health stress. Therefore, let it be hypothesized that the effect should increase with increasing average age of the propositi, other things being equal. The predicted pattern of effects thus will take this age factor into account.

And finally, let it be hypothesized that household sex distribution is a conditioning circumstance. If most of the propositi are females, then the existence of a health problem stress might well cause a greater change in the lives of the propositi than if more males are present in the household. For example, in a husband and wife household, if the husband comes down with illness, it might be necessary for the wife to change from housewife to breadwinner, and the transition might result in health problems for the wife. Also, the female is often thought to be more dependent on other members of the household for her sense of security; if illness in the household were to disturb that sense of security, health problems might result. Thus, let it be hypothesized, in accord with the stress idea, that the effect, *ceteris paribus*, should be greater for predominantly female propositus households.

Now we come to the specification of the prediction in accord with the hypothesized conditioning influences of household size, age and sex distribution. There are essentially two problems encountered here:

(1) specification of the relative values of the prediction for various levels of each conditioning factor. For example, in respect to household size, should the index be inversely linearly related with number of propositi, or should the index decrease in some other way as number of propositi increases?

(2) specification of the manner in which the various conditioning factor effects (effects of size, age, sex) are to be combined. For example, is it predicted that the effects of household size, age and sex are additive

[1] Those, to whom the *ceteris paribus* clause constitutes a red flag, should be advised that the truth of the statement that other things are equal will be tested.

or multiplicative, or do they interact in some more or less complicated way?

At this point, it would be quite helpful to have data from previous studies at hand. Then it could be decided better what the relative levels of the prediction index should be. In the absence of such information, some arbitrary (or intuitive) specification becomes necessary in order to arrive at a single prediction index.

It is noted, here, that one could refuse to predict any more than, for example, these three things:

(1) the effect will increase with decreasing number of propositi, for given categories of average age and sex distribution;

(2) the effect will increase with average age, for given propositus household size and sex distribution;

(3) the effect will increase as the proportion of female propositi increases, for given size and age categories.

This form of semi-quantitative prediction may have some merit (Feigl, 1953), but it cannot meet the criteria we have set down. This prediction, if tested, would permit one to determine either that it agreed or disagreed with observations. Either the prediction would agree in every respect with the observed effects or it would not. But there would be no question as to the significance of agreement and disagreement components of variation. This could not be tested, because no basis would have been provided for separating the agreement and disagreement components of variation in the effect.

We are forced, then, in the absence of prior data, to specify somewhat arbitrarily both the relative levels of the index for various levels of each factor and the manner in which effects of the three factors are to be combined. This state of affairs does, indeed, indicate that the causal hypothesis is not so well conceived that predictions of quantitative functional relationships automatically ensue. But we also note that the more arbitrary any single testable prediction index may be, the less reason (*a priori*) there is for the prediction to be successful. If, by fortunate coincidence, the prediction is successful, then it may be carried over to subsequent studies in which case the suitability of the initially arbitrary parts of the prediction would be tested again.

In the present illustration we take the following index values as our prediction of the pattern of effects for the indicated size, age, sex distribution categories:

SIZE	VALUE	AVERAGE AGE	VALUE	SEX DISTRIBUTION [2]	VALUE
1	4	15-29	0	M	0
2	2	30-44	1	F	4
3	1	45-54	2		
4 & up	0	55 & up	4		

As our rule for combining effects of the different factors, we make the assumption that additivity of effects holds. Thus, for example, the predicted index score for propositus households of size 4, average age 15-29, predominantly male, is $0+0+0=0$; for propositus households of size one, age 55 or over, female, the index score is $4+4+4=12$; and so on.

The index score for the α^{th} size-age-sex category is denoted by C_α. All the C_α scores are shown in the second-last column of table 2. Table 2 also shows the observed serial relation, r_α, for each of the 22 categories being tested.[3] By inspection of table 2, there appears to be some degree of agreement between prediction and obsrvation. For the lower index scores, 5 and below, negative serial relations predominate, while for the index scores higher than 5, positive relations predominate. But by the procedures illustrated in detail in the following sub-section, it is found that the agreement component of variation is not significantly great; agreement as great or greater would occur about 33 times in a 100 by chance alone. Thus, the prediction does not account for a significant amount of variation in the serial relations.

Also by the analysis in the following sub-section, the residual variation (the disagreement component) is found to be well within the realm of chance variation.

Detailed Analysis of Variation In The Partial Serial Relation of Household Health Problems

The observed partial association, r_α, is taken to be distributed approximately as a normal distribution with variance equal to $1/n_\alpha$, where n_α is the size of a simple random sample from the α^{th} population, when n_α

[2] A propositus household is considered to be predominantly female (F) if more than half of the propositi are female; otherwise, the household is considered to be predominantly male (M).

[3] Size-age-sex specific categories for which $n_\alpha < 30$ are excluded. This is because the approximation of the sampling distribution of r_α to a normal distribution, with variance equal to $1/n_\alpha$ is poor when n_α is small. (Sheehe, 1959).

TABLE 2

Comparison of prediction (index score) with observed partial serial relation for size-age-sex specific groups of propositus households *

α	SIZE	AGE	SEX	n_α	INDEX (C_α)	r_α
1	5 & up	15-29	M	158	0	—.043
2	4	15-29	M	143	0	+.196
3	4	30-44	M	96	1	—.208
4	5 & up	30-44	M	57	1	—.175
5	3	15-29	M	104	1	—.074
6	2	15-29	M	135	2	—.040
7	3	30-44	M	99	2	—.038
8	3	45-54	M	33	3	—.322
9	2	45-54	M	124	3	—.043
10	5 & up	15-29	F	92	4	—.085
11	2	45-54	M	97	4	—.046
12	4	15-29	F	54	4	+.029
13	3	15-29	F	117	5	—.109
14	1	30-44	M	30	5	—.025
15	5 & up	30-44	F	45	5	+.101
16	2	55 & up	M	179	6	—.114
17	3	30-44	F	97	6	+.078
18	3	45-54	F	42	7	+.013
19	1	55 & up	M	59	8	+.045
20	3	55 & up	F	35	9	+.038
21	1	45-54	F	36	10	+.000
22	1	55 & up	F	72	12	+.052

* The serial relation, r_α, has been adjusted for the influence of certain interviewer characteristics and for sample strata; hence the use of the term, partial serial relation (Sheehe, 1959).

is in the neighborhood of 50 or more (Sheehe, 1959). This statistical property proves very useful in the analysis of variations in the partial relation among a number of sub-populations. The analysis of total variation, the test of significance (or confidence interval) for the mean partial relation, the test of significance of variations about the mean, the test of significance for the agreement of prediction with observation, and the test of significance for residual variations, is a part of a unified whole. The following analysis is closely analogous to the routine analysis of variance in experiments. The only technical difference is that, in the usual experiment, the "error" variance is estimated, and ratios of two chi-squares are formed in F tests of significance, while in the following

TABLE 3

Basic computations for analysis of variations (see text)

(1)	(2)	(3)	(4)	(5) (2)×(3)	(6) (2)×(4)	(7) (3)×(5)	(8) (4)×(6)	(9) (4)×(5)
α	n_α	r_α	C_α	$n_\alpha r_\alpha$	$n_\alpha C_\alpha$	$n_\alpha r_\alpha^2$	$n_\alpha C_\alpha^2$	$n_\alpha C_\alpha r_\alpha$
1	158	—.043	0	—6.794	0	.292	0	0
2	143	.196	0	28.028	0	5.493	0	0
3	96	—.208	1	—19.968	96	4.153	96	—19.968
4	57	—.175	1	—9.975	57	1.746	57	—9.975
5	104	—.074	1	—7.696	104	.570	104	—7.696
6	135	—.040	2	—5.400	270	.216	540	—10.800
7	99	—.038	2	—3.762	198	.143	396	—7.524
8	33	—.322	3	—10.626	99	3.422	297	—31.878
9	124	—.043	3	—5.332	372	.229	1116	—15.996
10	92	—.085	4	—7.820	368	.665	1472	—31.280
11	97	—.046	4	—4.462	388	.205	1552	—17.848
12	54	.029	4	1.566	216	.045	864	6.264
13	117	—.109	5	—12.753	585	1.390	2925	—63.765
14	30	—.025	5	—.750	150	.019	750	—3.750
15	45	.101	5	4.545	225	.459	1125	22.725
16	179	—.114	6	—20.406	1074	2.326	6444	—122.436
17	97	.078	6	7.566	582	.590	3492	45.396
18	42	.013	7	.546	294	.007	2058	3.822
19	59	.045	8	2.655	472	.119	3776	21.240
20	35	.038	9	1.330	315	.051	2835	11.970
21	36	.000	10	.000	360	.000	3600	0
22	72	.052	12	3.744	864	.195	10368	44.928
Sum X	1904	X	X	—65.764	7089	22.335	43868	—186.371
Average				r_{ave} —.03454	C_{ave} 3.7232	.01173	23.039	—.09788
Product Average				r_{ave}^2 .001193	C_{ave}^2 13.861			$(r_{ave})(C_{ave})$ —.1286

analysis, the "error" variance (of the measures of partial association) is "known," so that chi-square tests of significance are performed.

The basic computations are set down in table 3. α denotes a particular size-age-sex specific sub-population of the Arsenal Health District; n_α is the number of observed sample elements from the α^{th} sub-population ;and r_α is the observed partial association. These are shown in the first three columns of table 3. In the fourth column of table 3, C_α is

listed. This is the index of predicted level of partial relation, as developed previously.

Column (5) is the product of entries in columns (2) and (3), $n_\alpha r_\alpha$. Column (6) is the product of (2) and (4), $n_\alpha C_\alpha$. Column (7) is (3)$\times$(5), $n_\alpha r_\alpha^2$. Column (9) is (4)$\times$(6), $n_\alpha C_\alpha^2$. Column (9) is the covariance column, the product of (4) and (5), $n_\alpha C_\alpha r_\alpha$.

There are 22 rows, one for each of the 22 sub-populations under analysis. The 22 entries in each column, with the exception of columns (1), (3) and (4), are summed to give the "Sum" row. Thus,

$$\sum n_\alpha = n = 1904; \quad \sum n_\alpha r_\alpha = -65.764; \quad \sum n_\alpha C_\alpha = 7089;$$
$$\sum n_\alpha r_\alpha^2 = 22.335; \quad \sum n_\alpha C_\alpha^2 = 43867; \quad \text{and} \quad \sum n_\alpha C_\alpha r_\alpha = -186.371.$$

Now, columns (5) through (9) are divided by $n = 1904$ to give the "Average" row. Thus,

$$\sum n_\alpha r_\alpha / n = r_{ave} = -.03454; \quad \sum n_\alpha C_\alpha / n = 3.7232; \quad \sum n_\alpha r_\alpha^2 / n = .01173;$$
$$\sum n_\alpha C_\alpha^2 / n = 23.039; \text{ and } \sum n_\alpha C_\alpha r_\alpha / n = -.09788.$$

Below the "Average" row, the "Product Averages" r_{ave}^2, and $(r_{ave})(C_{ave})$ appear.

Note that $r_{ave} = -.03454 = -3.5\%$. This is the adjusted relation of household health problems, adjusted for household size, age, sex and for stratum and interviewer characteristics.

Also note that $\sum n_\alpha r_\alpha^2$ equals 22.335. This is distributed, under the null hypothesis, as a chi-square with 22 degrees of freedom and is found to be non-significant. Thus, the 22 partial relations do not vary significantly from zero. Now a test of the significance of the mean, r_{ave}, can be performed. The total chi-square with 22 degrees of freedom is made up partly of variation due to the mean and partly of variation about the mean. Variation due to the mean is

$$n r_{ave}^2 = 1904(.001193) = 2.271.$$

This is a chi-square with one degree of freedom under the null hypothesis, and it is not found to be significant on the 5% level. Thus, the observed mean, $r_{ave} = -3.5\%$, is not significantly different from zero.

Now the variation about the mean is found by subtracting variation due to the mean from the total variation. Hence, variation about the mean is

$$\sum n_\alpha r_\alpha^2 - n r_{ave}^2 = 22.34 - 2.27 = 20.07,$$

and is distributed as a chi-square with 22 minus 1 = 21 degrees of free-

dom under the null hypothesis that there is no universe variation about the mean. Again, on referring 20.07 to a chi-square table with 21 degrees of freedom, the observed variation about the mean is far from significant.

Now we wish to decompose the variation about the mean, 20.07, into two components: the first component, with one degree of freedom, is that portion of the variation which is predicted; the second component, with 20 degrees of freedom, is the residual unpredicted variation. First, we obtain the slope of the regression of r_α on C_α by:

$$\begin{aligned}\text{slope} &= \operatorname{cov}(r_\alpha, C_\alpha)/s_{C_\alpha}{}^2 \\ &= (\textstyle\sum n_\alpha C_\alpha r_\alpha/n - r_{ave}C_{ave})/(\sum n_\alpha C_\alpha{}^2/n - C_{ave}{}^2) \\ &= [-.0979 - (-.1286)]/(23.039 - 13.861) = .0307/9.178 \\ &= .00334.\end{aligned}$$

This slope, .00334, is the slope of a weighted least squares line of agreement which could be drawn on a scatter diagram of observed effect (r_α) versus prediction score (C_α). In order to determine the amount of variation in r_α due to the slope in the line of agreement, it is merely necessary to multiply the squared covariance of (r_α, C_α) by n, and divide by the variance of C_α, thus:

$$n(\operatorname{cov} r_\alpha, C_\alpha)^2/s_{C_\alpha}{}^2 = 1904(.0307)^2/9.178 = .195.$$

This component of variance, .195, is distributed as a chi-square with one degree of freedom on the null hypothesis. The test of significance, however, should not be performed by reference to a chi-square distribution, because such a test is two-tailed. In the case of testing the prediction for agreement with observations, we are concerned with discriminating between a positive slope and a negative slope; hence we wish to test whether the slope is significantly positive. Therefore, taking $\sqrt{.195} = +.44$, we get a standard normal deviate (positive because the slope is positive). On referring $+.44$ to the normal table, we find that a value of $+.44$ would be exceeded 33 times in 100. Thus, the slope is far from being significantly positive, and it is concluded that the amount of agreement of prediction with observed variations is not significant.

Finally, the residual variation, not accounted for by prediction, is $20.07 - .195 = 19.87$. On the null hypothesis, this is distributed as a chi-square with 21 minus one, or 20 degrees of freedom, and it is found to be far from significant. Then it is concluded that there is not a significantly great variation left unaccounted for by the prediction.

The analogy between the foregoing analysis and the analysis of variance can be brought out clearly by summary in a table of variations (table 4).

TABLE 4

Analysis of variations in r_a

SOURCE OF VARIATION	D.F.	OBSERVED CHI-SQUARE	PROBABILITY
Total ($\sum n_a r_a^2$)	22	22.34	.5 > P > .3 not sig.
Due to mean (nr_{ave}^2)	1	2.27	.2 > P > .1 not sig.
About the mean	21	20.07	.7 > P > .5 not sig.
In agreement	1	.20	.7 > P > .5 not sig. (one-tailed normal)
In disagreement	20	19.87	.5 > P > .3 not sig.

Discussion and Conclusions

From the foregoing analysis, we can conclude that, when household size, average age, and sex distribution, and when possible bias due to sample strata or interviewer characteristics are accounted for, the serial relation was not greatly different from zero. The observed negative serial relation, —3.5%, shows that, more likely than not, the incidence of second-year health problems for propositus households with initial health stress was actually slightly less than for propositus households without initial stress.

But it has been emphasized that the level of this relation is not the relevant consideration in testing our causal hypothesis. This is because there is always the possibility that some factor or combination of factors, other than those specifically taken into account, can produce the observed level of association. In formulating the prediction, we have not ruled out the possibility that unspecified positive familial forces or negative selective forces might have tended to increase or decrease, respectively, the observed effects. Firstly, we can reason that there were unspecified environmenal and genetic forces acting on all or several members of a household; if a health problem showed up in one member of the household in the first year because of these familial forces, the same forces may have produced health problems in the remaining members (propositi) in the second year. This, then, would have tended to produce positive serial relations. But, offsetting these possible familial forces, selective forces acting on the different individuals within a household may have been in operation. It could be that those individuals who had health

problems in the first year were, in general, "susceptibles," so that the remaining propositi were relatively resistant individuals. When households consisting of such propositi were compared to households without first year health problems (households in which susceptible individuals had not already been selected out), the serial relation may have tended to be negative. To sum up, the very occurrence of a first year health problem may have been evidence of the operation of familial forces while, concomitantly, it may have set up negative selective influences because of individual differences of household members. The negative serial relation which we have actually observed (−3.5%), indicates that negative influences predominated. But this is not germane to the causal hypothesis and the corresponding prediction which has been formulated. Neither would a significantly positive average serial relation confirm, nor a significantly negative average serial relation disprove, the stress hypothesis which has been formed.

Rather, the focus has been on variations in the level of the serial relation among the size, age, and sex specific groups of households. This variation about the mean was found to be non-significant. But, again, the mere presence or absence of significant variation about the mean is not directly a criterion for accepting or rejecting the causal hypothesis. It is true that, if there had been a significantly high variation in the level of the serial relation, we could agree that "something was happening" among the size-age-sex specific classes of households, but we could not conclude that this "something" was in whole or in part the stress of initial household health problems. Conversely, just because variation of the serial relation was not significantly great, we cannot conclude that initial health problem stresses played no part in creating the variation.

In order to put the causal hypothesis to a really discriminating test, we must make a prediction based on that hypothesis. We must predict that certain factors (in our example, household size, average age and sex distribution) are important conditioning variables which affect the level of the serial relation. Further, we must predict the manner in which these conditioning variables affect the serial relation, other things being equal. Finally, we must adjust for any additional conditioning variables which, it is anticipated, might vitiate the *ceteris paribus* clause. (In our example, strata and interviewer characteristics are such additional variables).

With a prediction of the above form at hand, we can proceed to make the test. Variation about the mean is decomposed into two components

(see preceding section and table 4): (1) the amount of agreement with the predicted index score and (2) residual variation.

If the prediction is successful in securing significant agreement and a non-significant residual, then the test is met. The causal concept has resulted in a successful prediction. Observed variations in levels of relation are consistent with the prediction; and further, observed disagreement with the prediction is consistent with the assumption that unspecified factors, not adjusted for in the analysis, constitute a random process. The assumption, that residual variation is a random disturbance, is the statistical equivalent to the classical assumption that "other things are equal." Hence, a test of the assumption, by determining whether or not there is significant residual variation, is a test of the truth of the *ceteris paribus* clause which was injected into the formulation of the prediction. This latter test is necessary in order to discriminate between a causal and non-causal interpretation. This is because, in the event of a significant amount of agreement with prediction, a significant residual variation would favor the interpretation that the prediction had merely "picked up" a portion of the significant but unexplained variation.

In our particular case, while there is not a significant residual, neither is there a significant amount of agreement. Then the test has not been met. It is therefore concluded that the concept of health problems as a stress producing, on average, additional subsequent health problems in the household has not been substantiated. If the test had been met, the causal concept would have been acceptable. Acceptance would imply that the causal hypothesis, as framed in detail, could remain essentially unchanged in further studies. On the other hand, rejection implies that the hypothesis is inadequately formulated; it should be revised before further studies are made.

SUMMARY

In view of the absence of control and randomization in observational studies, a stringent test of predictions based on causal concepts has been proposed. As applied to a prediction based on the concept of health problems, in general, as cause for increased subsequent health problems in the household, the test was not met; therefore, this causal hypothesis, in the framework of this study, was not substantiated.

ACKNOWLEDGMENT

I am grateful to Dr. Antonio Ciocco and to Dr. Donovan Thompson for their many helpful suggestions.

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DEMOGRAPHIC ASPECTS OF THE POPULATION OF HUMAN AUTOPSIED CASES AS REPORTED IN THE UNITED STATES, 1955 *

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OFTEN an investigator finds himself in a position where he wishes to make useful and valid generalizations about a living population from data that can be obtained only from information on autopsied cases. Since the performance of an autopsy is not legally mandatory in the case of every death which occurs in the United States, data obtained solely from autopsied cases could lead to erroneous inferences. To realize the danger inherent in such a procedure, one needs only to recall that data obtained from autopsied cases alone are not data obtained from a probability sample of a living population but rather from a selected sample of a deceased population (figure 1). In fact, even if all persons dying were autopsied, there would be considerable risk of error in drawing conclusions about the living population on the basis of data obtained only from the dead cohort.

On the other hand, demographers, pathologists, statisticians, and others engaged in certain types of research are faced with the practical problems of planning and analyzing studies based upon data obtainable only from autopsied cases. Therefore, a description of the population of autopsied cases in terms of selected demographic characteristics might be useful to these investigators. Because such a description seems not to have been made conveniently available by demographers, a study was undertaken in an attempt to bring some information to bear upon this subject.

* Indebtedness is expressed to the National Office of Vital Statistics (NOVS) for the special tabulation, particularly to Dr. I. M. Moriyama, Chief, Mortality Analysis, for his assistance; to the author's associates in biostatistics, Frances A. Norton, Carolyn A. Saunders and Suzanne S. Thomas for cartographic and computational assistance; and to many other colleagues at the L. S. U. School of Medicine and elsewhere for stimulating suggestions and for criticizing the manuscript. Needless to say, the author alone is responsible for the errors, shortcomings and interpretations.

General Objective of the Study

The problem of making valid inferences to a living population based upon data stemming only from autopsied cases is somewhat like attempting to relate a purposive sample (n) to an unknown parent population (N). However, having recognized the difficulty of such an undertaking, its true import will be disregarded until later and the present attention given to the overall objective of this study which is as follows: to provide a description of autopsized cases with regard to some of the more common

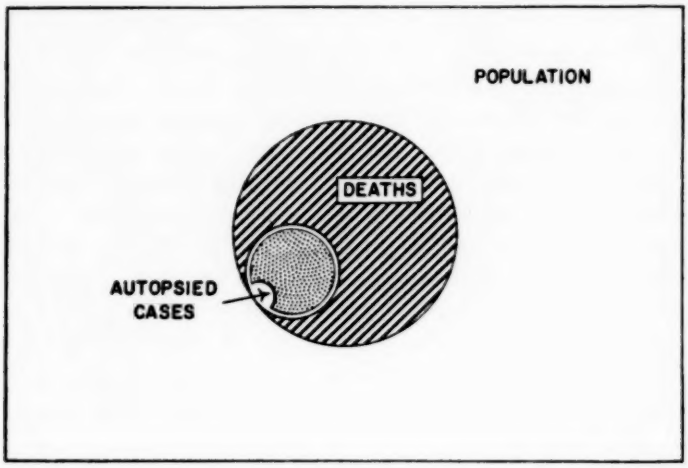

FIGURE 1. SYMBOLIC REPRESENTATION OF AUTOPSIED CASES AMONG DEATHS IN A SPECIFIED POPULATION DURING A GIVEN PERIOD OF TIME.

demographic characteristics as well as to analyze the selectivity which seems to have operated in the "choosing" of persons to be autopsied. It should be noted that the concern is not with how an autopsy was performed or with its completeness or technical aspects, but rather with the demographic characteristics of a reported population of autopsied cases which was generated.

Purpose and Scope of This Paper

This particular paper has set itself the limited task of providing a general overview or frame of reference by describing the nature of the data as to whether or not an autopsy was performed on each person who died in the United States during a single calendar year, 1955.

AUTOPSIED CASES REPORTED IN THE UNITED STATES, 1955

Definition of Autopsy

For the purposes of this paper, an autopsied case is one for which the standard certificate of death has been checked "yes" in answer to the question, "Was autopsy performed?" In addition, use has been made of reports from certain hospitals indicating the number of autopsies performed relative to the number of persons dying in those hospitals.

Universe of Autopsied Cases, 1955

In 1955, about 17.8% of all death certificates in the United States indicated that an autopsy had been performed. However, more than one-sixth of the death certificates furnished to the National Office of Vital Statistics (NOVS) failed to indicate whether or not an autopsy was performed. In spite of the latter, a special tabulation of the universe of more than 272,000 reported autopsied cases was obtained from the NOVS and serves as the basis for this paper.

The particular calendar year, January 1—December 31, 1955, was selected because the cards (used in processing the data for this year) had been punched to include a code which specified the autopsy status.

Limitations of the Data

The practice of reporting autopsy status on death certificates varies considerably among the states. Whether or not an autopsy was performed was reported on more than 98% of the death certificates in Arizona in 1955 while this fact was reported on less than 42% of the death certificates in Montana (for color-sex comparisons, see table 1). It is clear from figure 2 that, with few exceptions, these data are reported the least frequently in southern states.

OBSERVATIONS BASED UPON DEATHS REPORTED AS AUTOPSIED CASES

If one is still willing to seek some tentative conclusions in the face of such stringent limitations of the data, it appears from data that were reported that relatively fewer autopsies were performed in the South and that certain western states autopsied the greatest percentages of those dying (figure 3). In the light of such a high percentage of "unknowns," these data are suggestive only (it should be noted that the number of cases for which autopsy status was not reported, 287,825 cases, was larger than the number of reported autopsied cases). However, it is interesting

TABLE 1

Percentage of deaths reported as autopsied cases and percentage for which autopsy status was not reported, by color and sex, United States and each state, 1955

STATE	PER CENT OF DEATHS REPORTED AS AUTOPSIED CASES				PER CENT OF DEATHS NOT REPORTED AS TO AUTOPSY STATUS			
	White		Nonwhite		White		Nonwhite	
	Male	Female	Male	Female	Male	Female	Male	Female
United States	*19.7*	*14.5*	*22.6*	*17.1*	*17.1*	*18.2*	*27.1*	*30.0*
Alabama	10.0	6.2	9.1	6.0	45.2	45.3	52.7	56.2
Arizona	29.7	22.3	25.2	18.8	1.3	1.3	3.2	2.5
Arkansas	9.7	6.2	9.2	4.7	30.7	31.3	42.2	44.1
California	37.0	25.2	49.0	38.5	3.5	3.4	2.7	3.0
Colorado	30.2	25.7	43.8	39.6	8.1	9.8	7.2	9.0
Connecticut	23.2	17.9	32.7	35.2	13.2	13.9	11.6	12.4
Delaware	24.4	20.2	38.7	33.1	16.3	18.7	11.6	10.7
District of Columbia	37.9	28.5	45.4	36.5	25.1	34.1	22.4	33.4
Florida	19.5	14.0	19.5	14.1	11.9	12.6	17.4	18.5
Georgia	12.3	8.4	10.1	6.4	31.5	34.4	35.2	39.6
Idaho	15.7	13.6	16.3	20.0	17.2	18.1	11.6	20.0
Illinois	19.9	15.9	35.8	30.0	5.8	6.4	4.4	4.6
Indiana	13.8	9.5	27.4	18.7	22.9	25.3	22.2	27.0
Iowa	13.3	9.2	26.0	21.9	19.7	20.8	13.6	7.3
Kansas	15.3	11.4	25.0	20.6	17.3	18.2	15.0	16.4
Kentucky	9.4	7.1	12.7	8.8	25.1	26.9	25.3	27.4
Louisiana	18.1	13.1	21.9	16.7	36.5	39.3	42.6	44.8
Maine	12.9	8.9	16.7	16.7	32.1	34.7	20.8	16.7
Maryland	24.6	16.9	37.0	27.1	26.8	33.8	27.4	35.7
Massachusetts	19.5	14.6	31.2	26.0	4.9	4.9	4.5	4.7
Michigan	21.0	16.7	30.8	26.6	10.8	12.4	9.3	10.9
Minnesota	22.7	18.8	32.7	33.8	18.8	19.5	11.1	10.1

TABLE 1—*Continued.*

	PER CENT OF DEATHS REPORTED AS AUTOPSIED CASES				PER CENT OF DEATHS NOT REPORTED AS TO AUTOPSY STATUS			
	White		Nonwhite		White		Nonwhite	
	Male	Female	Male	Female	Male	Female	Male	Female

Minnesota	22.7	18.8	32.7	33.8	18.8	19.5	11.1	10.1

TABLE 1—*Continued.*

STATE	PER CENT OF DEATHS REPORTED AS AUTOPSIED CASES				PER CENT OF DEATHS NOT REPORTED AS TO AUTOPSY STATUS			
	White		Nonwhite		White		Nonwhite	
	Male	Female	Male	Female	Male	Female	Male	Female
Mississippi	8.6	4.2	4.6	2.0	38.1	40.5	51.5	52.9
Missouri	19.7	14.6	34.7	28.3	17.7	20.4	16.9	17.9
Montana	9.8	8.3	9.6	3.4	57.6	58.4	70.7	69.7
Nebraska	16.3	11.7	32.8	26.7	16.8	16.6	7.8	5.8
Nevada	21.5	17.3	18.8	18.5	4.1	4.0	4.0	1.2
New Hampshire	16.6	12.7	14.3	50.0	25.7	25.9	28.6	0.0
New Jersey	20.3	14.3	30.3	23.3	19.9	22.8	22.4	25.1
New Mexico	18.8	12.6	19.4	11.3	17.0	18.4	15.6	13.9
New York	21.1	15.3	36.6	30.0	14.5	15.1	15.3	15.8
North Carolina	13.2	9.8	9.3	6.4	27.1	28.8	31.9	34.8
North Dakota	21.1	17.3	16.0	28.2	16.2	16.6	8.6	25.6
Ohio	18.7	13.8	34.3	29.3	15.7	17.0	15.2	18.5
Oklahoma	9.0	6.2	11.5	10.3	32.6	33.5	35.4	32.8
Oregon	26.2	21.4	37.7	34.1	5.4	6.5	4.5	4.1
Pennsylvania	18.3	12.8	38.9	32.3	16.9	19.1	15.9	19.3
Rhode Island	17.8	12.8	33.0	24.6	16.3	20.0	8.0	13.0
South Carolina	13.0	9.2	10.4	7.2	34.2	36.0	41.3	43.1
South Dakota	14.2	10.3	13.0	10.5	19.2	19.3	24.9	21.8
Tennessee	10.1	6.7	11.1	6.7	40.5	43.5	55.4	58.2
Texas	15.0	10.7	18.8	12.3	21.8	21.7	26.0	27.1
Utah	18.2	14.5	23.1	16.3	27.4	28.1	33.3	39.5
Vermont	17.0	12.5	33.3	0.0	20.0	21.0	33.3	0.0
Virginia	18.8	13.8	16.1	11.5	18.0	19.5	19.5	22.8
Washington	23.4	18.9	33.3	31.5	18.7	20.6	14.7	16.3
West Virginia	11.8	8.4	15.8	10.5	28.7	30.4	30.4	31.4
Wisconsin	18.2	13.5	35.2	28.4	16.6	18.9	12.1	10.9
Wyoming	18.7	16.6	15.2	27.0	16.4	15.7	41.3	24.3

Source: **Unpublished data from the National Office of Vital Statistics, 1959.**

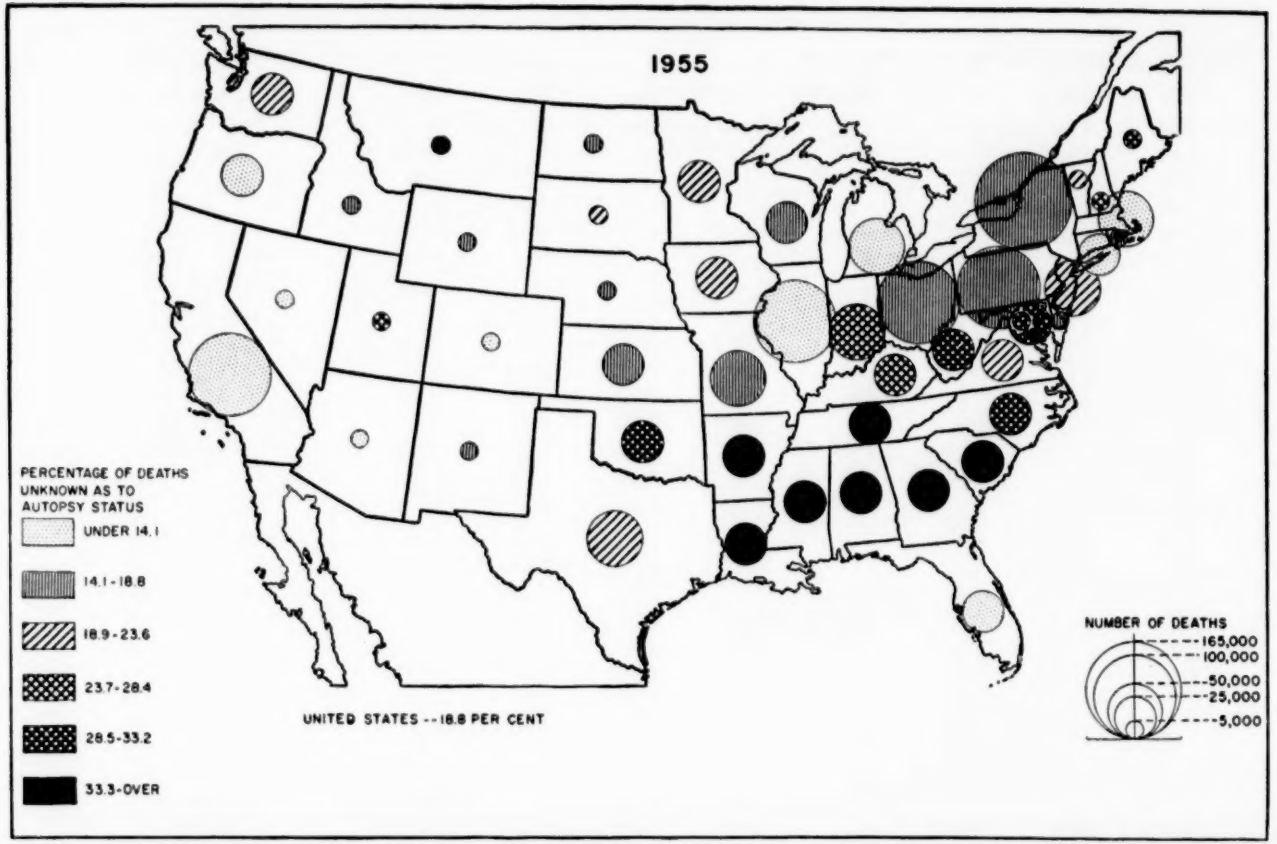

FIGURE 2. PERCENTAGE OF TOTAL DEATHS FOR WHICH AUTOPSY STATUS WAS NOT REPORTED, UNITED STATES, 1955. (*Source of data*: Unpublished data from the National Office of Vital Statistics.)

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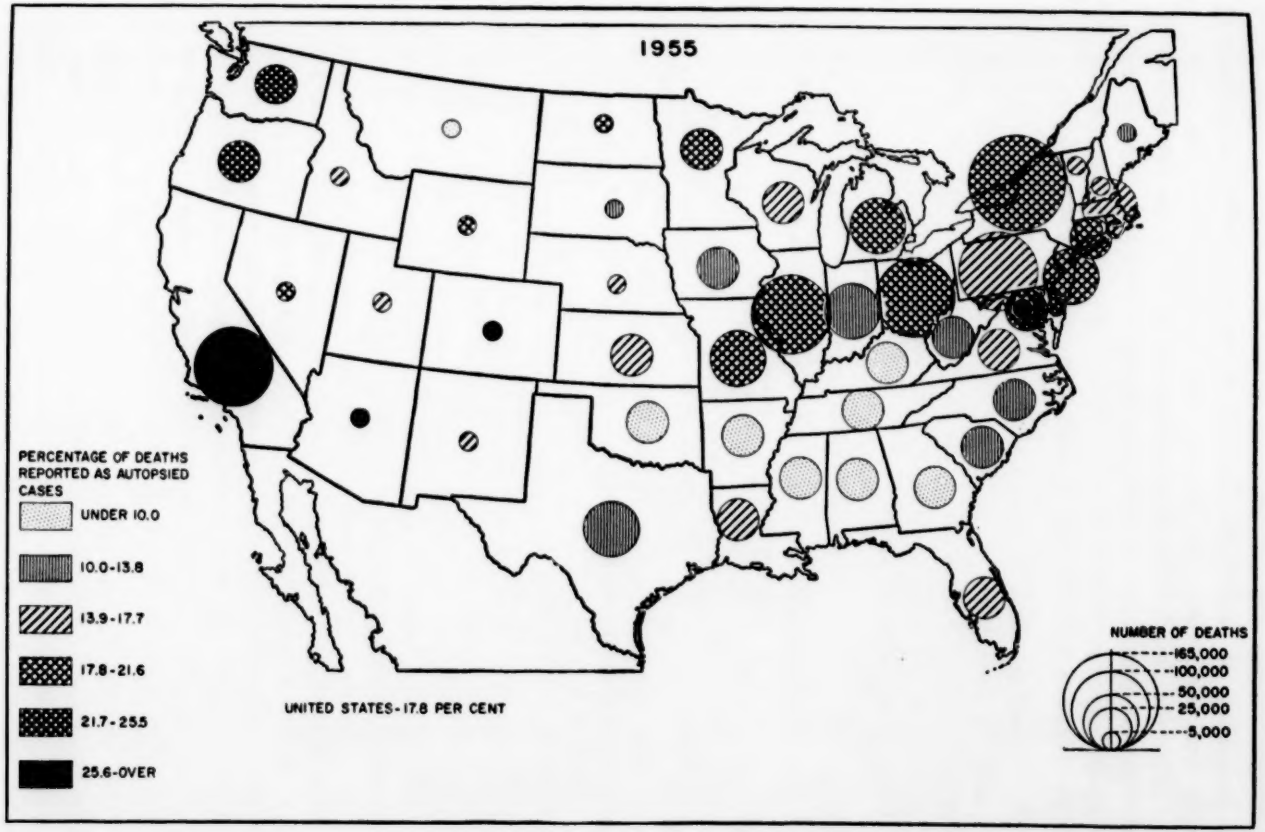

FIGURE 3. PERCENTAGE OF REPORTED AUTOPSIED CASES AMONG ALL DEATHS, UNITED STATES, 1955. (*Source of data*: Unpublished data from the National Office of Vital Statistics.)

to note that there was a distinct tendency for states which autopsied a high percentage of those dying likewise to report whether or not an autopsy was performed. In fact, a rank-order correlation of $+.71$ ($P < .001$) was found between percentage of total deaths reported as autopsied and percentage of deaths reported as to whether or not an autopsy had been performed (for the sake of brevity, persons who die and are autopsied will often be referred to as "deaths autopsied").

Sex. From the data of reported autopsied cases, it appears that a dead male is more likely to be autopsied than a dead female. This observation holds true generally in the various states among both whites and nonwhites. In fact, it holds true in every state for whites and in all except seven states for nonwhites.

TABLE 2

Hospital deaths and autopsies, by major type of service, continental United States, 1956

TYPE OF SERVICE OR OWNERSHIP	NUMBER OF DEATHS EXCLUDING STILLBIRTHS	PERCENTAGE OF DEATHS AUTOPSIED
Total	646,923	36.9
Short-term general and special	550,421	35.7
Long-term general and special	16,816	29.6
Psychiatric	38,369	24.9
Tuberculosis	4,785	36.5
Federal	36,532	70.7

Source: *American Hospital Association* (1957).

The effect of unreported autopsy status on the above findings is not clear. One could speculate that unreported data might not materially affect the findings since (a) it would seem that if a death receives enough attention for an autopsy to be performed, it is likely to be reported as an autopsied case; and (b) there is no obvious reason why there should be a great differential in the completeness of such data by sex.

Color. For the United States, nonwhite persons appear to be autopsied following death in somewhat greater proportions than white persons. However, the percentage of white male deaths in which an autopsy was reported exceeded that of nonwhite male deaths in 14 states, and the

percentage of white female deaths reported as autopsied exceeded the percentage of nonwhite female deaths in 11 states.

A Comparison with Autopsied Cases among Hospital Deaths, 1956

In 1956, 1,564,476 deaths were reported in continental United States (NOVS, 1958). More than 41% of all these deaths occurred in hospitals which reported to the American Hospital Association (table 2). Nearly 37% of those dying in such hospitals were reported as being autopsied. Thus it would appear, as one would expect, that the proportion of deaths autopsied in these hospitals is much greater than the minimum of 18% reported on death certificates in 1955 for the whole United States. It is of interest, however, to note that even in hospitals approved for internship training the proportion of autopsied cases is highly variable; the fraction of deaths reported as autopsied cases ranges from less than one-fourth to more than nine-tenths (Council on Medical Education, 1958).

Speculation as to Differentials among States in Reported Autopsy Status

Data lending themselves to tests for plausible explanations of the differentials in unreported autopsy status or in the rates of reported autopsied cases, by states, were not readily available for this study. Nevertheless, many overlapping factors suggest themselves as possibly contributing to these differentials: different rates of violence; different interests (of physicians, families, communities, hospital administrators, insurance companies and the like); different traditions including religious beliefs; rural-urban differences; variations in the quality of medical facilities; variations in the ratio of physicians to population; variations in per capita income by state; variations in the policies of state departments of health; as well as many others. In fact, one could speculate that reported death rates from selected diseases are associated with the reported rate of autopsied cases. One might articulate one of his hunches somewhat as follows: states which have the highest per capita income report the greatest proportion of deaths as being autopsied. Similar intuitive statements could be made for states with the highest proportion of urban population or for states with the highest ratios of physicians to population. Other variables which might have explanatory value could be considered in a similar manner.

As a crude test of such speculation, the possible importance of some such hypothetical factors was "tested" by ranking the states according to the following composite or catch-all factors:

F_1 = percentage of deaths reported as autopsied cases (NOVS, 1959);

F_2 = percentage of deaths for which autopsy status was not reported (NOVS, 1959);

F_3 = estimated per capita buying power in 1955 (SM, 1956);

F_4 = number of physicians per 100,000 population in 1955 (Census, 1959);

F_5 = percentage of the population classified as urban in 1950 (Census, 1952);

F_6 = death rate per 100,000 population assigned to arteriosclerotic heart disease, including coronary disease (420), 1954-1956 (NOVS, 1956, 1957, 1958; Census, 1957);

F_7 = death rate per 100,000 population assigned to accidents (E800-E962), suicide (E963, E970-E979), and homicide (E964, E980-E985) 1954-1956 (NOVS, 1956, 1957, 1958; Census, 1957).

Then Spearman rank correlation coefficients (r_S) were computed giving the following results (Siegel, 1956):

FIRST FACTOR	SECOND FACTOR	r_S	LEVEL OF SIGNIFICANCE
F_1	F_3	.66	$P < .001$
F_1	F_4	.64	$P < .001$
F_1	F_5	.64	$P < .001$
F_1	F_6	.31	$.01 < P < .05$
F_1	F_7	—.23	$.10 < P < .20$
F_2	F_3	—.62	$P < .001$
F_2	F_4	—.46	$.001 < P < .01$
F_2	F_5	—.52	$P < .001$
F_2	F_6	—.35	$.01 < P < .05$
F_2	F_7	.11	$.40 < P < .50$

Obviously the foregoing provide no definitive answers but they do suggest areas which might merit further exploration. It may be worthwhile to make two comments. (a) It appears that factors F_3, F_4 and F_5 tend to measure the same phenomenon. This is supported by the value of the coefficient of concordance, $W = .82$, uncorrected for ties, with a level of significance of less than .001 under the hypothesis of no association among the three factors. There is a high degree of relationship between percentage of the population classified as urban by the Bureau of the Census,

F_5, and physician ratio to population, F_4, ($r_S = .77$); percentage urban, F_5, and per capita income, F_3, ($r_S = .80$); as well as substantial relationship between per capita income, F_3, and physician ratio to population, F_4, ($r_S = .61$). In all three cases $P < .001$. (b) In view of the association referred to earlier between proportion of deaths autopsied and autopsy status reported, the reversal in sign of the statistically significant coefficients is not surprising.

A General Observation Concerning Data Obtained on Autopsied Cases

Most of the data utilized in this paper were produced by our "national reporting system" of vital statistics; that these data have many of the limitations of survey data is well-known. However, it is probably worthwhile to observe that research studies based upon human autopsied cases likewise should be classified as "survey research" and not as "experimental research."

SUMMARY

This study attempts to define more clearly the group of dead persons which results from a complex combination of vital and social processes and becomes reported as the population of autopsied cases. In order to provide a frame of reference, data on autopsied cases for the calendar year 1955 have been examined crudely. The evidence is not sufficient to justify even tentative conclusions but the data do lend statistical support to the following hypotheses: (H_1) a smaller proportion of those who die in southern states is autopsied as compared to the proportion autopsied of those who die in other sections of the United States; (H_2) dead males are more likely to be autopsied than dead females; (H_3) nonwhite persons who die are more likely to be autopsied than white persons who die; and (H_4) states which rank high in wealth, percentage of the population classified as urban, and availability of physicians tend to rank high in the proportion autopsied.

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THE WAVE OF ADVANCE OF AN ADVANTAGEOUS GENE: THE SICKLE CELL GENE IN LIBERIA

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THE clines in the frequency of the sickle cell gene which are found in many tropical and sub-tropical regions of the Old World are among the most striking in human genetics. In some areas such as East Africa these clines are closely associated with the present distribution of falciparum malaria. Since it now seems quite conclusive that this disease is responsible for the high frequencies of the sickle cell gene, these clines in East Africa could be called stable, although, of course, this stability depends on the malaria conditions remaining constant. On the other hand, the clines for the sickle cell gene in West Africa do not appear to be associated with the present distribution of falciparum malaria and hence could be called unstable. Since the malaria conditions necessary to maintain high frequencies of the sickle cell gene are more widespread than the high frequencies of this gene, I have postulated (Livingstone, 1958) that at present the gene is advancing through these areas where conditions favorable to high frequencies exist. Liberia is one area where such an advance seems to be occurring. In the northwestern part of this country the tribes have about 20% carriers of the sickle cell gene, while in southeastern Liberia the frequency is essentially zero. From northwestern to southeastern Liberia there is a rather smooth gradient in the frequency of the sickle cell gene when the intervening populations are sampled by tribe. However, since 80% of the marriages occur within the town and each tribe contains many towns, most tribes in Liberia undoubtedly contain several breeding isolates. Thus, the tribal frequencies are the averages of several isolate frequencies which may well be significantly different. The purpose of this paper is to present further data on the distribution of the sickle cell gene within some of the larger tribes of Central Liberia among whom the frequency declines most abruptly and to explore further the factors involved in determining the nature of this cline.

* National Science Foundation Postdoctoral Fellow.

TABLE 1

The frequency of the sickle cell gene in the paramount chiefdoms of the tribes of Central Liberia and in the tribles of other regions of Liberia

TRIBE	PARAMOUNT CHIEFDOM	NUMBER EXAMINED	NUMBER POSITIVE	SICKLE CELL TRAIT (%)	SICKLE CELL GENE FREQUENCY
Kissi	Tamba Taylor	459	99	21.57	.108
Gbandi	Boymah Jollah	421	62	14.73	.074
Mende	All in Sierra Leone	16	4	25.00	.125
Mende	All in Liberia	110	18	16.36	.082
Vai	All	114	17	14.91	.075
Gola	All	268	31	11.57	.058
Loma	Guzeh	143	16	11.19	.056
Loma	Tellewoyan	62	7	11.29	.056
Kpelle	Gleh	59	8	13.56	.068
Kpelle	Kpangbai	344	63	18.31	.092
Kpelle	Tarkono	76	12	15.99	.080
Kpelle	Fahn Gwilly	53	1	1.89	.009
Kpelle	Steven Giddings	82	16	19.51	.098
Kpelle	Kole Gwee	43	5	11.63	.058
Kpelle	Wea Wea	66	4	6.06	.030
Kpelle	Swar Gbanyah	65	5	7.69	.038
Kpelle	Doloken Paye	123	3	2.44	.012
Kpelle	Lango Lipaye	37	7	18.92	.095
Kpelle	Southwest Chiefdoms [1]	20	4	20.00	.100
Kpelle	Bassa Chiefdoms [2]	20	2	10.00	.050
Bassa	Menyongar	32	5	15.63	.078
Bassa	Northern Chiefdoms [3]	40	10	25.00	.125
Bassa	Garbudu	48	7	14.58	.073
Bassa	Mamba	76	6	7.89	.039
Bassa	Buchanan and vicinity	23	6	26.09	.130
Bassa	Frank Yarsee	42	2	4.76	.024
Bassa	Central Chiefdoms [4]	50	1	2.00	.010
Bassa	Southern Chiefdoms [5]	53	0	0	0
Mano	Bona-Sua	199	3	1.51	.008
Mano	Yennigen	102	0	0	0
Dei	All	54	2	3.70	.019
Gio	All	522	9	1.72	.009
Kru	All	196	1	0.51	.003
Krahn	All	186	1	0.54	.003
Grebo	All	123	1	0.81	.004
Webbo	All	178	1	0.56	.003
Americo-Liberians		110	17	15.45	.077

[1] Holder, Todee, Mt. Barclay, Mt. Coffee.
[2] Menyongar, Nathan Paye, Nardeh, Vogar, Garbudu, J. Diggs.
[3] Nathan Paye, Nardeh, Vogar.
[4] Korpuwi, J. Diggs, Gbi Doru.
[5] Dehgar, Timbo, River Cess.

METHODS AND MATERIALS

The methods used in these investigations are the same as those of previous investigations on the frequency of the sickle cell gene in Liberia (Livingstone, 1958). The great majority of the subjects tested were rubber tappers on the Firestone Plantation, but individuals attending the out-patient clinic of the Liberian Institute of Tropical Medicine were also tested. In addition, individuals who were tested on other surveys

FIGURE 1. Percentage incidence of the sickle cell trait in the tribes of Liberia. (The Mamba, Grand Bassa, and River Cess figures within the Bassa tribe represent earlier estimates of the cline within that tribe based on smaller numbers.)

in various parts of Liberia and on whom the necessary data were obtained are also included. Since no significant differences were detected between the methods of sampling in previous investigations, the results of these various surveys have been combined here without further testing.

RESULTS

In table 1 are shown the frequencies of the sickle cell trait and the sickle cell gene for the paramount chiefdoms of the tribes of Central Liberia and for the tribes of other areas of Liberia. Some of the paramount chiefdom samples were quite small, so that the samples from

adjacent ones have been combined in some instances. Since some of the samples are so small, some of the variation could be attributed to chance. However, chi-square tests on the frequency of the sickle cell trait among the chiefdoms of the Kpelle and among the chiefdoms of the Bassa are both highly significant; whereas for the Loma and Mano tribes these tests

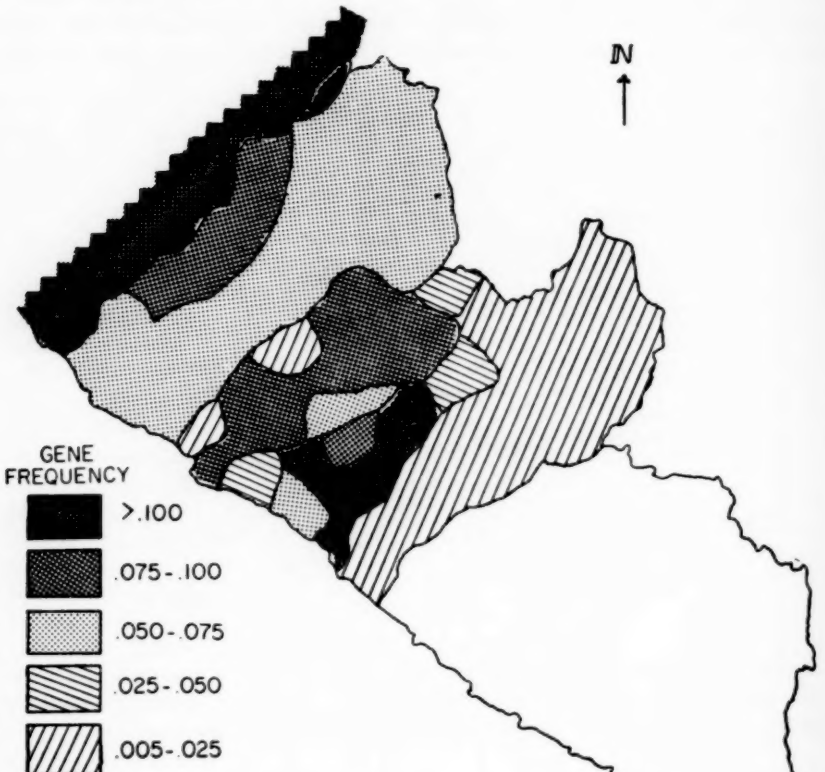

FIGURE 2. The cline in the frequency of the sickle cell gene in Liberia.

are not significant. But despite the non-significance of this test for the Mano, all positives for this tribe were found in Bona Sua's chiefdom, which is the most northerly and borders the Kpelle tribe; whereas there were no positives in Yennigen's chiefdom, which also borders the Kpelle but is closer to the Gio and other tribes further south that exhibit low frequencies of the sickle cell gene. The location of the tribes of Liberia

and their average frequencies of the sickle cell trait are shown on Figure 1. Figure 2 is an attempt to show the cline in the frequency of the sickle cell gene as it is indicated by the groupings shown on table 1.

DISCUSSION

It can be seen that the sampling of the tribes of Central Liberia by paramount chiefdom has uncovered significant variability in the frequency of the sickle cell gene among the isolates within the Bassa and Kpelle tribes. It should be noted, however, that the data presented in this paper do not represent samples of isolates. Although the paramount chiefdoms are closer in size to the actual isolates than the tribes and may be in the process of becoming isolates, they still contain on the average 10 towns and a total population of about 10,000. In a census of 400 marriages I have found that about 80% of these marriages occurred within the town, 10% within the paramount chiefdom, and the remaining 10% either inter-paramount chiefdom or inter-tribal depending on the nature of the borders of the groom's paramount chiefdom. Hence the paramount chiefdom contains about 10 isolates each with an effective population size of perhaps 500.

In any case, the smooth cline in the frequency of the sickle cell gene which resulted from the tribes being sampled as units now appears to be much more erratic. In southeastern Liberia, where the gene is almost completely absent, there could be little variability between isolates in its frequency; whereas in northwestern Liberia and Sierra Leone, which is to the north of Liberia, no studies have been done on the variability in the frequency of the sickle cell gene between villages, chiefdoms, or other sub-tribal units. However, Allison (1956) in Freetown, which is in north coastal Sierra Leone, and Rose and Suliman (1955) in the far southwestern interior of Sierra Leone obtained similar frequencies for the Mende, and Allison (1956) also found the frequency among the Creole and Timne to be similar to that of the Mende. In addition, studies of the tribes of Guinea to the north of Sierra Leone have found frequencies among the Fula and Susu similar to those in Sierra Leone Neel *et al.*, 1956; Leite and Re, 1955). These studies seem to indicate that the variability between tribes or chiefdoms is not as marked in these areas where the gene frequency is close to equilibrium. Thus, significant intra-tribal variability may well be a feature of those areas with populations in which the sickle cell gene has recently begun its rapid rise toward equilibrium. Since these intermediate frequencies are very unstable, greater variability among such populations would be expected.

Of the factors which can contribute to gene frequency change, the shape of this cline in the sickle cell gene seems to be determined for the most part by two of them, gene flow and selection, although with isolates of this size gene drift cannot be ruled out entirely. But because of the great differences in fitness of the various genotypes for this gene, gene drift would appear to have less effect on the sickle cell than on other genes. The amount and direction of gene flow has been determined to a great extent by unique historical events, and these explain some of the features of this cline. For example, the high frequencies along the lower course of the St. John River (Bassa tribe of Buchanan and vicinity) are perhaps due in part to the fact that this area was both the site of a large slave trading station and later of considerable settlement by the Americo-Liberians. On the other hand, despite the effects of these unique factors, it seems to me that certain generalizations can be made about the relative importance of the two factors, gene flow and selection, in determining this cline. If there were a considerable amount of gene flow between adjacent populations and most of the gene flow occurred between populations a short distance from each other, then the shape of the cline would be relatively smooth. If, on the other hand, there were much less gene flow and this occurred sporadically and over great distances, then the cline would be more erratic, and one would expect to find neighboring populations with quite different frequencies of the gene. Although the paramount chiefdoms of the Kpelle and Bassa contain several isolates, the great differences in frequency among them do seem to indicate that the latter model is more appropriate for this part of the wave of advance of the sickle cell gene. Thus, it appears that the spread of the high frequencies of the sickle cell gene in this part of West Africa is due for the most part to the action of selection operating on the few sickle cell genes which have been introduced into each population.

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BOOK REVIEWS

Growth Diagnosis: Selected Methods for Interpreting and Predicting Physical Development from One Year to Maturity. By LEONA M. BAYER AND NANCY BAYLEY. 241 pp. University of Chicago Press, Chicago. 1959. $10.00.

This attractive book on child development provides a well-organized battery of measurements and ratings of size, shape and physical maturity. Physicians and others may use it to define a child's status relative to explicit norms for North American White children, mainly of North European ancestry and reared in circumstances favoring rapid growth, large body size and few debilitating diseases. The first author is a physician, the second author a psychologist and human biologist. Few living workers have so successfully worked on both the psychology and the somatology of the young as Bayer and Bayley.

In a developmental battery, the number of possible somatic measurements and observations is enormous, and the choice of a minimal, representative sampling is debatable. The present list defines many events below the neck, but excludes the head and face. Anyone who proposes such a diagnostic technique should make few demands on the technical skill of possible users, call for cheap and simple measuring instruments, utilize a minimal number of body build photographs and X-ray films, and yet observe critical somatic events at critical ages.

On this basis, the Bayer-Bayley battery seems at least partly defensible and reasonable. On the living child, the measurements include weight, stature, sitting height, and the widths of shoulders (biacromial) and hips (bicristal). These last three dimensions are not for the unskilled, but reveal discrepancies in the lengthening of the limb bones, and measure the broadening of shoulders and hips in adolescence as criteria of somatic masculinity or femininity.

To me, developmental assessment should include biologically rather distinct tissues as much as possible and I would favor a more explicit treatment of the subcutaneous adipose layer. A standardized skinfold caliper is one good way to measure it, and another is a standardized X-ray film of the chest (Garn and Gorman 1956, Human Biology *28*: 407-413). The Bayer-Bayley method antedates some of the current interest in nutriture and body composition in children.

The authors briefly discuss the rating of bone age from the hand and wrist, and justly refer the reader to the second edition of the *Radiographic Atlas of Skeletal Maturation* (*Hand*) by Greulich and Pyle. A single X-ray film of this region is now known to be highly representative of the developing postcranial skeleton in general.

The head, on the other hand, is so markedly independent and complex that it may well require a battery in itself. In detail, this region would seem to be chiefly of interest to specialists such as orthodontists. The counting and classifying of teeth, however, could have been included even in a book such as the present one.

Bayer and Bayley advocate the taking of nude full-length body build photographs, even though adequate work space for such photography is often unavailable. They also favor the "loose" pose of the arms, which is not so suitable for photographic measurements and does not reveal muscularity and hyperextension of the elbow as fully as the more rigid "somatotyping" pose. In my experience, even most six-year-olds can be photographed in the rigid pose with brief and skilful coaching.

The book contains the fullest available description of the Bayer-Bayley method of assessing somatic masculinity or femininity ("androgyny") from photographs. I consider this chapter very useful indeed, especially for work on adolescents. The photographic standards for rating pubic hair, genital and breast maturation in general are not as well reproduced as those in Tanner's *Growth at Adolescence*, which Bayer and Bayley fail to cite in their bibliography.

This volume is mainly the fruit of several very well-planned longitudinal growth studies in northern California. It ought to be within easy reach of everyone with a broad interest in child development. I doubt whether the entire battery is likely to be used except in endocrine clinics, but parts of it can be useful to a considerable diversity of specialists in the biology of the young.

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Diferencias Sexuales en el Hueso Coxal. By SANTIAGO GENOVÉS TARAZAGA. 550 pp. Publicaciones del Instituto de Historia, Universidad Nacional Autonoma de México, Mexico 20, D. F. Primera serie, Num. 49, 1959. No indication of price.

Sex is such an important determinant of virtually all measurements and characteristics of bones that, whatever the questions at issue, one of the first steps in any study of skeletal materials from archaeological excavations must be the classification of the material according to sex. The value of conclusions concerning racial history or other problems will largely depend on the degree of accuracy in the ascription of sex. Thus, for instance, if all doubtful cases are classed as males (and many wrongly so), the population (both males and females) will be thought to have been of smaller, more delicate physique than was actually the case. Although, on the average, sex affects most attributes of bones, individual bones of males and females are frequently difficult or impossible to distinguish.

This study of sex differences in the hip bone is the published version of a Cambridge doctoral thesis and has all the advantages of detailed workmanship, exhaustive treatment of the literature, and full documentation associated with such a dissertation. It suffers from common faults of dissertations, however: long and unessential (although often interesting) digressions, occasional repetitions, multiplicity of problems handed, contentiousness (at least by the standards considered appropriate in the United States), and lack of sharp focus. Nevertheless, this work is essential for serious investigators of the question of sex differences in the skeleton. They will find 10 chapters, 2 appendices, 53 figures of all types, 120 tables of data, over 300 references, and an index.

Dr. Genovés made 36 measurements and some 13 morphological observations on each of 759 unpaired exhumed hip (innominate) bones. Of these bones 33 were from known males and 40 from known females from the cemetery of St. Bride, London, and 23 from males and 26 from females of known sex from a cemetery at Schooten near Bruxelles, Belgium. The remaining 637 were from unidentified individuals from St. Bride and were sexed anatomically and independently of the investigation here reported.

The technique of making each measurement is fully described, illustrated and compared with other possible methods which have been used. The results are presented separately for males and females for the two series of known sex and for various subseries of unknown sex. Tables

of data show number measured, mean and its standard error, range, and standard deviation with its standard error for each of 36 measurements and 9 indices (including, among others, height/width of ilium, pubic/ischial length, width/length of the obturator foramen, depth/width of the iliac fossa, depth/width of greater sciatic notch, acetabular width/pubic length). Morphological traits are presented as of masculine, doubtful or feminine type for males and females separately. Genovés applies to the metrical data a simplified form of discriminant function (which makes the assumption of little intercorrelation between measurements). The index of the sciatic notch, the iliac length, the anterior-posterior length of the auricular facet, the distance from the supra-acetabular point to the anterior border of the greater sciatic notch, the vertical diameter of the acetabulum and the symphyseal-obturator width of the pubis can together correctly discriminate the sex of about 95% of hip bones.

For the morphological traits, Genovés divided the percentage of males rated masculine in respect to each trait by the percentage rated feminine and uses the logarithms of these ratios (and of similar ones for females) to construct a point system for weighting morphological traits. In this way it was also possible to indicate the sex correctly for about 95% of the hip bones.

A method of combining metrical and morphological methods is devised. Of the 122 hip bones of known sex, the same 7 are misclassified by this technique as by morphology alone. Three of these are also misclassified by the metric method, but the other four are among bones too fragmentary to classify metrically.

In addition to his analysis, Genovés gives a full historical review and discussion of sex differences not only in the hip bone but also in the pelvis as a whole and in other bones. In his critical remarks concerning techniques Genovés favors criteria which can be defined precisely and repeated closely. This generally leads him to prefer geometric descriptions, such as maximum and minimum distances, to the use of morphological landmarks such as the synostosed junctures between the ilium, ischium and pubis.

Dr. Genovés does not believe (as others have sometimes claimed) that any single trait or index can give the sex of a hip bone with a high degree of probability. He distrusts all claims for a high degree of certainty in deducing sex from material of the type he studied.

The author's statistical tests of sex give 95% correct answers in the material of known sex. The performance is even somewhat better on

the undocumented bones. In this material, however, there may be a few males with perfectly "good" female pelves in most respects or vice versa. Such errors would remain undemonstrated and the sex of these specimens would be erroneously listed as "correct."

It is to be regretted that the summary does not repeat the formulae giving the best available indices of sex distilled from the great number of characteristics and combinations tested by the author. It remains for someone to prepare a brief guide for the use of physical anthropologists and archaeologists who wish to identify the sex of skeletons from hip bones. That would, of course, be quite a different sort of book, and its author would do well to lean heavily on the work under review; at least all those who wish to determine the sex (and also, incidentally, the age) of skeletons could learn from Genovés' work the uncertainties which remain even after the most complete examinations.

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The Study of Population: An Inventory and Appraisal. Edited by PHILIP M. HAUSER and OTIS DUDLEY DUNCAN. xvi + 864 pp. University of Chicago Press, Chicago, 1959. $15.00.

This book, a truly ambitious undertaking, was commissioned by the National Science Foundation as part of its program of assembling information about the nation's scientific resources. The two editors solicited original contributions from 27 authors in addition to six chapters prepared by themselves.

The volume represents a combination of elder statesmen's observations on the state of the arts and the profession of demography, a series of profiles of the development of demography in different countries, an encyclopedia of substantive and methodological knowledge with an occasional textbook flavor, and a number of essays delineating the connections between demography and other sciences.

The first four chapters written by the editors review the status of demography as a science. For anyone interested in acquiring a clear, comprehensive picture of the orientations, scope, methods, and the profession of demography, these first hundred pages can be enthusi-

astically recommended. The main shortcomings of this entire section are a rather elaborate and, in the reviewer's opinion, futile attempt to distinguish "demography" (as an independent study of the size, distribution and composition of population and the components of change) from what the editors label "population studies" which use techniques of demographic analysis, but depend more on substantive theory from other disciplines. Such distinctions are highly unlikely to have any visible effect on the future course of the field's intellectual history. Following an excellent review of the bewildering variety of ways in which demographers have used the term "theory," another objection is provoked by the editors' somewhat contentious discussion of "psychosocial theories of fertility," or, more generally, the study of microparameters in population research. Perhaps students of motivation in fertility research have occasionally committed the crime of psychological reductionism as charged by the editors, but their general indictment of such research probably arises from a strong predilection for ecology displayed at various points in the book—a point of view incidentally which might find more sympathy among biologists than among sociologists. These criticsms, however, reflect mainly a difference in orientation between reviewer and editors, and should not detract from the fact that the book on the whole is a first-rate contribution.

The historical reviews of the development and status of demography in France, Great Britain, Germany, Italy, Brazil, India and the United States are highly informative, although inevitably superficial at many places and in part repetitious of the scholarly contribution by Lorimer who presents a general history of the field. Perhaps the most difficult assignment went to Irene Taeuber who contributed a fine description of developments throughout the entire heterogeneous Pacific area (including China and Japan). Her treatment is imaginative and the research questions she poses are provocative.

At the risk of unfairly neglecting a number of authors, all of whose contributions are praiseworthy, I shall select a few for special mention. Hawley's chapter on "Population Composition" is a neat, highly concentrated and clear presentation of some of the basic methodological and conceptual tools used by the demographer. Dorn's chapter on mortality is an excellent summary of this area and Ryder's piece on fertility is a really sophisticated presentation of both methodological and substantive aspects of research in this subject. These chapters are followed by a succinct review of reproduction rates by Hyrenius and an outstanding discussion of the field of internal migration by Bogue.

Biologists will be particularly interested in three chapters in the final section of the book which relate population research to various disciplines. Peter Frank contributed the chapter on "Ecology and Demography" in which demographic research on nonhuman populations is discussed. It is apparent from his presentation that in the study of population, the social and biological sciences have more methodological than theoretical common interests.

The biologist would also be interested in the essays by Spuhler, "Physical Anthropology and Demography" and the succeeding chapter by Kallmann and Rainer, both of which focus on population genetics. It is difficult to understand why these two chapters were not reversed in order since the latter defines concepts in genetics the knowledge of which is assumed in the former chapter.

At least two other chapters merit special attention. Duncan's chapter on the interrelation of human ecology and demography is undoubtedly the most comprehensive statement that can be made on the subject. And finally, Spengler's contribution is, in typical form, a thoroughly scholarly summary of knowledge arising from the interpenetrations of demography and economics.

The editors are to be heartily congratulated on this work. The very compilation of such an inventory reflects the fact that demography has come of age. A quick glance at estimated levels of the world's future population suggests that the field has a promising future.

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Body Build in a Sample of the United States Army. Part I: Body Build in Relation to Military Function. Part II: Measurements of Body Build. By E. A. HOOTON. 348 pp. Technical Report No. EP/102 of Environmental Protection Research Division, H.Q. Quartermaster Research and Engineering Command, U.S. Army Natick, Mass., 1959. No price.

This mimeographed volume consists of reprints of two reports originally made by Professor Hooton in 1948 and 1949, but given at that time very limited circulation. They concern the body build of

some 40,000 men at the time of their demobilisation from the United States Army in 1946. The study is known to human biologists through the publications of Randall (1949) and Newman (1952) in this and other scientific journals and the write-ups of the anthropometric measurements given by Newman and White (1951) in a government report. It provides, unfortunately, heaven-sent ammunition for those who argue against all research by large-scale surveys on the grounds that in them techniques and even ideas, like chemical preparations taken from the laboratory to the industrial plant, become inevitably diluted with the products of muddle and hazard.

Nude photographs, in front, side and rear views, after the manner of W. H. Sheldon, were taken on these men, together with a large number of body measurements, 13 of which are considered here. A new system of classifying build was used, derived from Sheldon's and sufficiently similar to it to confuse all but experts in this tiny field, while sufficiently different to provide in reality some rather dissimilar results. The credit for devising the new system is given to Dr. J. M. Andrews, and the medal for the really remarkable job of personally checking the ratings on all these thousands of pictures to Mr. F. L. Stagg. In retrospect, the similarity to Sheldon's system seems to have confused the author and his colleagues themselves, for it is not apparent from the text that much has been altered except that all mesomorphy ratings are 1 degree lower than Sheldon's, all endomorphy ratings a degree or so higher, and ectomorphy ratings given strictly according to height/$\sqrt[3]{\text{weight}}$, whereas Sheldon only follows this ratio to the extent of a correlation of about 0.9. Hooton still referred to his sets of ratings as "somatotypes," as did Newman also in 1952. Later studies of the two systems, in particular that of Howells (1957), showed that the new system differed in principle as well as in detail from Sheldonian somatotyping (Sheldon and others 1940; 1954), and it is now generally and correctly referred to as "Hooton body typing." No pictures are given in this volume, nor any directions worthy of the name for rating the first two components. These omissions constitute at present a complete bar to using the Hooton system.

Some critics have maintained that somatotyping—by which I mean assignment of ratings following Sheldon (1940, 1954)—cannot be learned from the published work alone. This is simply not true, at least in places remote from anthropological storm centres. I have recently had in my laboratory a Dutch physician studying growth who had familiarised himself with somatotyping purely from books and had practised for some years the rating of well-taken pictures. His ratings on some of my

pictures agreed with my previously given ones to half a unit or less in 90% of instances, just as did Dupertuis' ratings (Tanner, 1954). But the charge of unrepeatability outside one particular laboratory can certainly be laid at the door of the Hooton system as matters stand at present.

It seems that the chief difference between the systems is that Hooton rated visible fat deposit as component one, and to a large extent visible muscular mass as component two. Thus he took total *tissue composition* as the main criterion for the first two components, while Sheldon took *shape* of the body, which reflects tissue location as well as composition and also allows skeletal shape differences to enter into the first two components as well as the third. The ultimate relative usefulness of the two methods of approach remains to be seen; my colleagues and I have for the last four years been trying to develop a consistent and detailed classification based on the amounts of fat and muscle and the amount and shape of the skeletal frame, and we have had encouraging results in its use in relation to endocrinological function, a previously very speculative subject (Tanner, Healy and Whitehouse, 1959; Tanner, Healy, Whitehouse and Edgson, 1959). But the point is that if one classifies by tissue composition, then there is no excuse for not measuring the tissue objectively. Accurate and easily usable fat calipers are available, it is not impossible to obtain roentgenograms, and even without them muscle widths can at least be approximated. Hooton's system seems to me to fall between two stools. It deliberately forgoes the possible rewards of Sheldon's effort to see through the presented physique to the morphogenotype beneath, while not seizing the compensatory advantage of objective measurement of anatomically distinguishable tissues. For these reasons I think it likely to fall into disuse.

However this may be, the voluminous data under review contain some interesting facts and suggestions. It is clear that different jobs in the armed forces are associated with different builds. Fliers are more muscular than ground crew; combat infantry more muscular than men in the supporting services. Amongst military specialties maintenance men are both fat and muscular, gunners muscular, administration clerks weak in muscle and, reassuringly, supply men fatter than all the rest. The difficulty is to know the meaning of these findings since the factors of selection of unit by subject on entry, selective assignment and migration while in the forces, and differential living and working conditions during the time of service are all mixed up. No effort is made to allow for length of service or age, both of which differ from one group to

another, nor to consider whether the subject was a volunteer or draftee. From a practical Armed Forces' point of view this may not matter too much; Hooton compares life in the Army with the struggle for existence, and says the sorting of physiques to different jobs represents the results of a kind of natural selection (the densest gravitating to the front and the lightest to the rear, like medieval atoms). He draws the conclusion that it may be more efficient to assign men to jobs taking physique into account at the beginning, rather than to rely on the slow selective process later.

The relations between physique and civilian occupation prior to service, education received, and marital status are interesting. Students are linear and distinctly lacking is muscle; professional and semi-professional people also lack muscle. Service workers and operators, and craftsmen and foremen, on the other hand, are above average in muscle. Salesmen and clerks are below average in it. Relatedly, men who have received college or professional education are relatively lacking in muscle compared with those who passed only grade or high school. There is a good deal of published work on the relation of physique and choice of career, and all these findings are in agreement with the general consensus.

In discussing marital status an engaging bit of *gelerntamerikanisch* appears: ". . . submedium fat men of the better muscular developments," the author says severely, "tend to be excessively married." In fact, a lower proportion of the linear, less muscular men, than of the fat muscular men are married; but once again age and education are left uncontrolled. There is also a good deal of information on differences in national origin; for example, men of British extraction are lacking in fat, men of Slavic extraction are more richly blessed with it.

In Part II tables are given of means and standard deviations of height, weight, leg and arm length, and nine other measurements for each of the different body types. Some idea of the type components can be obtained from their relationships to the measurements; stature rises with increase of components one and three, leg and arm length rise with increase of component one, bideltoid rises only slightly with increase of component two. Finally, differences in measurements between Whites and Negroes are discussed. Negroes, compared with Whites assigned the same body type, are heavier, have longer legs and arms, wider shoulders, a shorter trunk, and a smaller chest circumference.

The data in this report are extensive, and it is probably worth while to have made them generally available. But there is little here that has not been demonstrated more precisely and effectively in smaller and

more critical studies. The pity is that many of the unique possibilities of these large-scale data have been left unrealised. When the survey was done modern computing machinery was not generally available; now it is, and analyses could be based on the original anthropometric measurements considered multivariately. Such analyses would be full of interest, and it is a tribute to the energy and enthusiasm of Hooton and his colleagues that the data exist on which they could be based.

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TANNER, J. M. 1954 Reliability of anthroposcopic somatotyping. Amer. J. Phys. Anthrop., *12*: 257-265.

TANNER, J. M., M. J. R. HEALY, AND R. H. WHITEHOUSE 1959 Fat, muscle and bone in the limbs of young men and women: their quantitative interrelationships studied radiologically. J. Anat., *93*: 563.

TANNER, J. M., M. J. R. HEALY, R. H. WHITEHOUSE AND A. C. EDGSON 1959 The relation of body build to the excretion of 17-ketosteroids and 17-ketogenic steroids in healthy young men. J. Endocr., *19*: 87-101.

The Human Integument. Edited by STEPHEN ROTHMAN. x + 260 pp. American Association For The Advancement Of Science, Washington, D. C., 1959. $6.75.

I have always suspected that the skin was the least understood organ because it was in the care of men who were so busy seeing patients that they had no time for research. It is really astonishing that the largest organ of the human body, and the one most exposed to the environment

should for so long have been regarded as a sort of covering for the really important parts of the body or, in the case of animal skin, as something out of which one made footwear, luggage, and lampshades. The nicely colored pictures of the cerebral hemispheres showing the large representation of cutaneous areas seemed merely to serve a decorative purpose, for nowhere else in the works in which such pretty pictures appeared was there adequate recognition of the fact that the skin was as highly complex an organ as all the evidence of experience suggested. What was wanting was the basic research on the human integument. During the last two decades that lacuna was being filled increasingly by workers attracted to the field of cutaneous physiology. Among the leading workers in this field is Stephen Rothman, the editor of the present volume.

The present volume is due to the sponsorship of the AMA, AAAS and the Society For Investigative Dermatology. There are twelve contributions as follows: R. B. Stoughton, "Relation of the Anatomy of Normal and Abnormal Skin to its Protective Function," R. D. Griesemer, "Protection against the Transfer of Matter Through the Skin," I. H. Blank, "Protection Against the Invasion of Bacteria and Fungi," B. W. Zweifach, "Structural Aspects and Hemodynamics of Microcirculation in the Skin," A. C. Burton, "Physiology of Cutaneous Circulation," R. R. Kierland, "Pathology and Therapy of Cutaneous Circulatory Disorders," E. J. Van Scott, "Significance of Changes in Philosebaceous Units in Acne and Other Diseases," A. L. Lorincz, "Biochemical and Hormonal Aspects of Sebaceous Secretion," M. B. Sulzberger, "Pathogenetic, Therapeutic and Cosmetic Considerations in Acne Vulgaris," A. W. Horton, "Etiologic Factors and the Pathogenesis of Premalignant and Malignant Lesions of the Skin," H. Pinkus, "Clinical, Histologic, and Differential Considerations," F. D. Malkinson, "Prognosis, Preventive Measures, and Treatment of Pre-malignant Conditions and Malignancies of the skin." There is an index.

It would be futile to discuss the merits of each paper in a short review. Each represents a valuable and stimulating contribution in its own right, and not the least valuable part of the volume are the discussions and bibliographies which follow each paper. Altogether this is a fundamental volume for anyone interested in the body's first line of defense.

In a future symposium it would be a good thing to consider skin pigmentation and subcutaneous fat.

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BOOK NOTICES

TEXTBOOK OF COMPARATIVE HISTOLOGY. By Warren Andrew. xix + 652 pp. Oxford University Press, New York, 1959. No price indicated. Systematic and broadly comparative. Microscopic structures are discussed according to organ systems.

EVOLUTION AND ANTHROPOLOGY: A CENTENNIAL APPRAISAL. viii + 171 pp. The Anthropological Society of Washington, Washington, D. C., 1959. No price indicated. A collection of essays reviewing the impact of evolutionary theory in the various sectors of anthropological sciences. Of special interest to the readers of *Human Biology* are likely to be the contributions of E. Mayr (biology), T. D. Stewart and J. S. Weiner (physical anthropology), A. T. Hallowell (behavior) and C. Kluckhohn's epilogue.

AMERICAN HANDBOOK OF PSYCHIATRY. Edited by Silvano Arieti. Two vols. xix + 2098 pp. Basic Books, New York, 1959. $25.00. A catholic portrait of problems, concepts, techniques, trends, and prospects of psychiatry. Of special interests are M. Ostrow's chapter on The Biological Basis of Human Behavior, B. Malzberg's Statistical Data, and F. J. Kallmann's Genetics of Mental Illness.

THE PROCESS OF AGING IN THE NERVOUS SYSTEM. Edited by James E. Birren. Henry A. Imus, and William F. Windle. xii + 224 pp. C. C. Thomas, Springfield, Illinois, 1959. $7.00. Proceeding of a conference aiming to summarize the present state of knowledge regarding the contributions of histology and histochemistry, biochemistry and physiology, study of behavior and functional neurology, and to seek new guide lines and approaches. The paper by H. E. Himwich reviews information on the chemical composition of the human brain.

THE HISTORICAL DEVELOPMENT OF PHYSIOLOGICAL THOUGHT. Edited by Chandler McC. Brooks and Paul F. Cranefield. xiii + 401 pp. Hafner, New York, 1959. $6.00. This is not a systematic history of physiology. Since these are proceedings of a symposium, one would hardly expect a systematic treatment. The symposium achieves excellence by its emphasis on integrative functions, both nervous and humoral, and on the dependence of medicine upon basic scientific thought.

THE HEINZ HANDBOOK OF NUTRITION. Edited by Benjamin T. Burton. viii + 439 pp. McGraw-Hill, New York, 1959. $5.75. A reference book covering the broad field of human nutrition. A chapter is devoted to obesity and leanness, and data on distributions of weight and height are given for boys and girls from 2 to 18 years, with information on the values of the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentile, provided by Professor Harold C. Stuart of Harvard University's School of Public Health.

THE FIFTH MENTAL MEASUREMENTS YEARBOOK. Edited by Oscar Krisen Buros. xxvii + 1292 pp. The Gryphon Press, Highland Park, New Jersey, 1959. $22.50. A boon to a wide variety of users of tests. The purpose of the volume is to assist in locating and evaluating tests, and to assemble critical reviews of books on mental measurements and the closely allied fields. The work is provided with five directories and indexes (periodicals, publishers, titles, names, and a classified index of tests).

RESEARCH TECHNIQUES IN HUMAN ENGINEERING. By Alphonse Chapanis. ix + 316 pp. The Johns Hopkins Press, Baltimore, 1959. $6.00. Human engineering is concerned with man as a component of man-machine systems. The present volume, practical in orientation and selective in coverage, deals with "those principles of human experimentation which are primarily useful in the (behavioral) study of men and machines."

ELEMENTARY DECISION THEORY. By Herman Chernoff and Lincoln E. Moses. xv + 364 pp. Wiley, New York, 1959. $7.50. Introduction into statistics conceived as the science of decision making under uncertainty. Concerned with the clarification of fundamental ideas underlying statistical methods, not with "how do you do it."

MEASUREMENT: DEFINITIONS AND THEORIES. Edited by C. West Churchman and Philburn Ratoosh. viii + 274 pp. Wiley, New York, 1959. $7.95. Proceedings of an AAAS symposium, held in December 1956. The first 2 sections deal with general aspects (meanings, theories) of measurement, the second 2 sections with problems of measurement in physics and in social sciences, respectively.

THE FOUNDATIONS OF HUMAN EVOLUTION. By Sir Wilfrid E. LeGros Clark. 74 pp. University of Oregon Press, Eugene, 1959. $1.00. The title of the last chapter characterizes well this small volume: "The lineage of mankind in rapid conspectus." The author appended a series of illustrations depicting the reconstruction forms of animals constituting the evolutionary history of the Primates.

RADIATION BIOLOGY AND MEDICINE. Edited by Walter D. Claus. xx + 944 pp. Addison-Wesley Publishing Co., Massachusetts, 1958. No price indicated. A series of authoritative reviews of selected aspects of the effects and uses of radiation in the life sciences. Especially relevant are the sections on the mutational effects of radiation and on mathematical biology. Reference is made, *passim*, to body composition.

HUMAN NUTRITION AND DIETETICS. By Sir Stanley Davidson, A. P. Meiklejohn, and R. Passmore. xii + 844 pp. Williams & Wilkins, Baltimore, 1959. $15.00. The volume is intended as a systematic presentation of the "newer knowledge" of nutrition. This is attested by the fact that the very first chapter deals with the composition of the body. The comprehensive character of the book is indicated by the section headings: Physiology, Food. Primary nutritional diseases. Nutritional aspects and dietary treatment of general diseases. Public health. Diet and physiological stress.

A TEXTBOOK OF GENERAL PHYSIOLOGY. By Hugh Davson. Second Edition. xvi + 846 pp. Little, Brown, Boston, 1959. $14.50. Revision (1st ed., 1951) of an outstanding treatise on those features of life that are common to all forms and thus are most fundamental, interpreted in terms of physics and chemistry.

CONCISE DICTIONARY OF SCIENCE. By Frank Gaynor. 546 pp. Philosophical Library, New York, 1959. $10.00. The title indicates the size, the subtitle the content: Physics, Mathematics, Nucleonics, Astronomy, Chemistry.

BIRTH N DEATH REGISTRATION IN MASSACHUSETTS 1639-1900. By Robert Gutman 115 pp. Milbank Memorial Fund, New York, 1959. $1.00. Portrays the developments from the rude beginnings of the registration system through the introduction and perfection of the system of modern vital statistics.

MODERN ORGANIZATION THEORY. Edited by Mason Haire. x + 324 pp. Wiley, New York, 1959. $7.75. "A group of (eleven) papers which are the ragged leading edge of a wave of theoretical development," focused on the organization of productive human groups. Biological models and concepts (homeostasis) are considered, together with a variety of other approaches.

THE FUNCTIONS OF THE ENDOCRINE GLANDS. By Peter F. Hall. xvii + 290 pp. Saunders, Philadelphia, 1959. $5.75. A readable presentation of endocrine physiology.

BIOLOGICAL AND BIOCHEMICAL BASES OF BEHAVIOR. Edited by Harry F. Harlow and Clinton N. Woolsey. xx + 476 pp. University of Wisconsin Press, Madison, 1958. $8.00. Proceedings of the Symposium on Interdisciplinary Research held at the University of Wisconsin. The 17 papers summarize outstanding ongoing programs of investigation concerned with the correlation of findings and methods of life "life sciences" (specifically, neuroanatomy, neurophysiology and neurochemistry) with the study of behavior. The chemical anatomy of the central nervous system is considered. The role of physique in behavior is not.

HISTORY AND PHILOSOPHY OE SCIENCE: AN INTRODUCTION. By L. W. H. Hull. xi + 340 pp. Longmans, Green, New York, 1959. $5.00. An attempt to "bridge the gap between science and the humanities by considering scientific ideas in a context of history and philosophy."

SIGMUND FREUD COLLECTED PAPERS. Edited and translated by Ernest Jones, Joan Riviere, Alix and James Strachey. Vol. 1, 359 pp.; Vol. 2, 404 pp.; Vol. 3, 607 pp.; Vol. 4, 508 pp.; Vol. 5, 396 pp. Basic Books, New York, 1959. $25.00 the set. This translation of Freud's *Sammlung kleiner Schriften zur Neurosenlehre* makes available a wealth of materials, written over a period of 45 long years (1893 to 1938), documenting the development of psychoanalysis as a theory, method, and movement.

INTERBEHAVIORAL PSYCHOLOGY. By J. R. Kantor. xvi + 276 pp. The Principia Press, Bloomington, Indiana, 1959. 2nd, revised ed. No price indicated.

The author is a behavioral theorist *par excellence* and he offers the present volume as a continuation of his efforts, initiated in *Principles of Psychology* (1924), "to forge naturalistic constructs (descriptions, interpretations) for psychological events." A chapter is devoted to the influences of biology on psychology and *vice-versa*.

PSYCHOPHARMACOLOGY FRONTIERS. Edited by Nathan S. Kline. xiii + 533 pp. Little, Brown, Boston, 1959. $10.00. Proceedings of a symposium held in connection with the Second International Congress of Psychiatry. While the core of the volume deals with highly specialized topics, the introductory section on Problems of Psychopharmacology is of a more general interest in connection with considerations of somatic therapies in psychiatry and etiology of mental disorders.

NOMOGRAPHY. By Alexander S. Levens. viii + 296 pp. Wiley, New York, 1959. $8.50. This is a second edition of a volume first (1937) published under the title *Alignment Charts*. A comprehensive treatment of widely applicable techniques used most frequently as time-saving devices in solutions of mathematical formulas and as a means for showing the interrelationships between variables.

STANDARDS OF NORMAL WEIGHT IN INFANCY. Ministry of Health Reports on Public Health and Medical Subjects No. 99. iv + 35 pp. Her Majesty's Stationery Office, London, (British Information Services, New York), 1959. 50¢. The standards, given separately for boys and girls, are based on data obtained in a survey involving close to 20,000 children and conducted in 1949/1950. Both attained weights and gains in weight from birth to the age of 3 years are considered. The zone of "normal variation" is defined by the 5th and 95th percentiles.

REPORT ON NATIONAL CONFERENCE ON THE LEGAL ENVIRONMENT OF MEDICAL SCIENCE. 114 pp. National Society for Medical Research, Chicago, 1959. No price is indicated. The 3 sessions dealt, respectively, with 1) Procurement of bodies for dissection, the use of cadavers, organ transplants, and autopsy procedures. 2) Animal experimentation. 3) Clinical research. A resource paper on "Medical research on human beings" (pp. 70-77) was contributed by Irving Ladimer.

BIOPHYSICAL SCIENCE: A STUDY PROGRAM. Edited by J. L. Oncley. viii + 606 pp. Wiley, New York, 1959. $6.50. A series of integrated lecture presentations on key problems (including gene action, radiobiology, nervous activity, and sensory performance but also bone mineralization and structure of muscle cells) and critical evaluations of recent advances. Designed "to aid and encourage the further blending of concepts and methods of physical science with those of life science in the investigation of biological problems."

TOOLS FOR MACHINE LITERATURE SEARCHING. By J. W. Perry and Allen Kent. Interscience Publishers, New York, 1958. $27.50. A comprehensive study

of an important new approach to the problem of retrieval of scientific information, with focus on "designing and applying electronic equipment to conduct searching, selecting and correlating operations directed to encoded non-numerical information."

INTERNATIONAL REVIEW OF NEUROBIOLOGY. Volume 1. Edited by Carl C. Pfeiffer and John R. Smythies. xii + 383 pp. Academic Press, Inc., 1959. $10.00. The rapid expansion of research on the biological bases of nervous function has demanded new media of publication. The aim of the Review "is to enable active workers in the fields of neurobiology (neurochemistry, neuroanatomy, psychopharmacology, psychology etc.) as well as those in biological psychiatry and neurology to give an account of recent progress in their fields."

THYROID HORMONES. By Rosalind Pitt-Rivers and Jamshed R. Tata. xiii + 247 pp. Pergamon Press Inc., New York, 1959. $7.50. A comprehensive summary of available information on the subject (close to 1800 references). The focus is on thyroid biochemistry and physiology but the latter is interpreted broadly and includes the treatment of such topics as effects on the central nervous system, growth, and goitrous cretinism.

THE HISTORY AND PHILOSOPHY OF KNOWLEDGE OF THE BRAIN AND ITS FUNCTIONS: AN ANGLO-AMERICAN SYMPOSIUM LONDON, JULY 15TH-17TH, 1957. Edited by F. N. L. Poynter. x + 272 pp. C. C. Thomas, Springfield, Illinois, 1958. No price is indicated. The symposium was planned as an historical introduction to the First International Congress of Neurological Sciences. It covers, in the form of 15 essays, much of the ground between Aristotle's considerations of body and soul, and the 20th century's accomplishments of bioelectronics and the promise of neurobiochemistry.

LES RÉGULATIONS PHYSIOLOGIQUES. By Eugène Schreider. 89 pp. Office International de Documentation et Librairie, Paris, 1958. No price indicated. In spite of its brevity, this is an important contribution to the biology of inter-individual differences and intra-individual variability. The subtitle indicates the focal point: An Attempt at a Biometric Revision of the Problem of Homeostasis.

MECHANISMS OF HYPERSENSITIVITY. Henry Ford Hospital International Symposium. Edited by Jos. H. Shaffer, Gerald A. LoGrippo, and Merrill W. Chase. xx + 754 pp. Little, Brown, Boston, 1959. $18.50. Provides a comprehensive picture of the fundamental mechanisms of allergic reactions. Of special interest is P. F. de Gara's critical review of the hereditary predisposition in man to develop hypersensitivity.

A HISTORY OF BIOLOGY TO ABOUT THE YEAR 1900. Third and Revised Edition. By Charles Singer. xxxvi + 380 pp. Abelard-Schuman, New York, 1959. $6.00. A new and completely revised edition of the outstanding general treatise (1st ed. 1931; 2nd ed. 1950), focused on the history of the great problems, including evolution, sex, development of the individual, and

mechanism of heredity. The motto: "L'histoire de la science, c'est la science même."

ANATOMY AND PHYSIOLOGY, VOL. 2: URINARY, RESPIRATORY, AND NERVOUS SYSTEMS, SENSATION AND SENSE ORGANS, ENDOCRINE AND REPRODUCTIVE SYSTEMS. By Edwin B. Steen, and Ashley Montagu. xix + 314 pp. Barnes & Noble, New York, 1959. $2.50. A summary published in the College Outline Series.

INFORMATION STORAGE AND RETRIEVAL: THEORY, SYSTEMS AND DEVICES. Edited by Mortimer Taube and Harold Wooster. xi + 228 pp. Columbia University Press, New York, 1958. $6.00. The phenomenal growth of the volume of scientific information makes the working scientist, not only the professional librarian, aware of the crying needs for storing information in ways that will permit an efficient recall of the stored material. The symposium, arranged by the Air Force Office of Scientific Research, reviews the technology and science of information storage and retrieval.

MULTILINGUAL DEMOGRAPHIC DICTIONARY (ENGLISH SECTION). viii + 77 pp. United Nations, Dept. of Economic and Social Affairs, New York, 1958. 50¢. The primary purpose of this dictionary, prepared by a Committee of the International Union for the Scientific Study of Population, is to facilitate translation of technical literature. It was published in an English, French and Spanish version, and consists of text in which the terms are described, supplementary notes, and an alphabetical index.

RADIATION, GENES AND MAN. By Bruce Wallace and Th. Dobzhansky. xii + 205 pp. Henry Holt, New York, 1959. $3.50. Aiming to be understandable to the general reader, the authors discuss the threat of genetic damage to man. While "the use of atomic energy opens before mankind vistas of unheard-of power, its misuse endangers his innermost nature."

BIBLIOGRAPHY OF MONOLINGUAL SCIENTIFIC AND TECHNICAL GLOSSARIES, VOLUME II: MISCELLANEOUS SOURCES. By Eugene Wuster. 146 pp. UNESCO (Columbia University Press, New York), 1958. $2.50. Arranged according to the Universal Decimal Classification. Contains subject, language, and author indexes.

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